# BEST AVAILABLE COPY

### Sequence Listing

<110>	de Sauvage, Frederic Carpenter, David A.
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Lys	Ala	Pro	Leu	Trp 35		Arg	Ala	Tyr	Phe 40		Gly	Leu	Leu	Phe 45
Ser	Leu	Gly	Cys	Gly 50		Gln	Arg	His	Cys 55		Lys	Val	Leu	Phe 60
Leu	Gly	Leu	Leu	Ala 65		Gly	Ala	Leu	Ala 70	Leu	Gly	Leu	Arg	Met 75
Ala	Ile	Ile	Glu	Thr 80		Leu	Glu	Gln	Leu 85	Trp	Val	Glu	Val	Gly 90
Ser	Arg	Val	Ser	Gln 95	Glu	Leu	His	Tyr	Thr 100	Lys	Glu	Lys	Leu	Gly 105
Glu	Glu	Ala	Ala	Tyr 110	Thr	Ser	Gln	Met	Leu 115	Ile	Gln	Thr	Ala	Arg 120
Gln	Glu	Gly	Glu	Asn 125	Ile	Leu	Thr	Pro	Glu 130	Ala	Leu	Gly	Leu	His 135
Leu	Gln	Ala	Ala	Leu 140	Thr	Ala	Ser	Lys	Val 145	Gln	Val	Ser	Leu	Tyr 150
Gly	Lys	Ser	Trp	Asp 155	Leu	Asn	Lys	Ile	Cys 160	Tyr	Lys	Ser	Gly	Val 165
Pro	Leu	Ile	.Glu	Asn 170	Gly	Met	Ile	Glu	Trp 175	Met	Ile	Glu	Lys	Leu 180
Phe	Pro	Cys	Val	Ile 185	Leu	Thr	Pro	Leu	Asp 190	Cys	Phe	Trp	Glu	Gly 195
Ala	Lys	Leu	Gln	Gly 200	Gly	Ser	Ala	Tyr	Leu 205	Pro	Gly	Arg	Pro	Asp 210
Ile	Gln	Trp	Thr	Asn 215	Leu	Asp	Pro	Glu	Gln 220	Leu	Leu	Glu	Glu	Leu 225
Gly	Pro	Phe	Ala	Ser 230	Leu	Glu	Gly	Phe	Arg 235	Glu	Leu	Leu	Asp	Lys 240
Ala	Gln	Val	Gly	Gln 245	Ala	Tyr	Val	Gly	Arg 250	Pro	Cys	Leu	His	Pro 255
Asp .	Asp	Leu	His	Cys 260	Pro	Pro	Ser	Ala	Pro 265	Asn	His	His	Ser	Arg 270

Gln Ala Pro Asn Val Ala His Glu Leu Ser Gly Gly Cys His Gly 275 Phe Ser His Lys Phe Met His Trp Gln Glu Glu Leu Leu Gly 290 Gly Met Ala Arg Asp Pro Gln Gly Glu Leu Leu Arg Ala Glu Ala 310 -Leu Gln Ser Thr Phe Leu Leu Met Ser Pro Arg Gln Leu Tyr Glu 320 His Phe Arg Gly Asp Tyr Gln Thr His Asp Ile Gly Trp Ser Glu 335 Glu Gln Ala Ser Thr Val Leu Gln Ala Trp Gln Arg Arg Phe Val 350 Gln Leu Ala Gln Glu Ala Leu Pro Glu Asn Ala Ser Gln Gln Ile 365 370 His Ala Phe Ser Ser Thr Thr Leu Asp Asp Ile Leu His Ala Phe 380 385 Ser Glu Val Ser Ala Ala Arg Val Val Gly Gly Tyr Leu Leu Met Leu Ala Tyr Ala Cys Val Thr Met Leu Arg Trp Asp Cys Ala Gln 415 Ser Gln Gly Ser Val Gly Leu Ala Gly Val Leu Leu Val Ala Leu 430 Ala Val Ala Ser Gly Leu Gly Leu Cys Ala Leu Leu Gly Ile Thr Phe Asn Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu Gly 460 Ile Gly Val Asp Asp Val Phe Leu Leu Ala His Ala Phe Thr Glu 475 Ala Leu Pro Gly Thr Pro Leu Gln Glu Arg Met Gly Glu Cys Leu Gln Arg Thr Gly Thr Ser Val Val Leu Thr Ser Ile Asn Asn Met 505 Ala Ala Phe Leu Met Ala Ala Leu Val Pro Ile Pro Ala Leu Arg 515 520 Ala Phe Ser Leu Gln Ala Ala Ile Val Val Gly Cys Thr Phe Val 530 Ala Val Met Leu Val Phe Pro Ala Ile Leu Ser Leu Asp Leu Arg 545 Arg Arg His Cys Gln Arg Leu Asp Val Leu Cys Cys Phe Ser Ser

Pro Cys Ser Ala Gln Val Ile Gln Ile Leu Pro Gln Glu Leu Gly 575 Asp Gly Thr Val Pro Val Gly Ile Ala His Leu Thr Ala Thr Val 590 Gln Ala Phe Thr His Cys Glu Ala Ser Ser Gln His Val Val Thr Ile Leu Pro Pro Gln Ala His Leu Val Pro Pro Pro Ser Asp Pro 620 Leu Gly Ser Glu Leu Phe Ser Pro Gly Gly Ser Thr Arg Asp Leu 635 Leu Gly Gln Glu Glu Glu Thr Arg Gln Lys Ala Ala Cys Lys Ser 650 Leu Pro Cys Ala Arg Trp Asn Leu Ala His Phe Ala Arg Tyr Gln 665 Phe Ala Pro Leu Leu Gln Ser His Ala Lys Ala Ile Val Leu 680 Val Leu Phe Gly Ala Leu Leu Gly Leu Ser Leu Tyr Gly Ala Thr 695 Leu Val Gln Asp Gly Leu Ala Leu Thr Asp Val Val Pro Arg Gly 710 715 Thr Lys Glu His Ala Phe Leu Ser Ala Gln Leu Arg Tyr Phe Ser 725 Leu Tyr Glu Val Ala Leu Val Thr Gln Gly Gly Phe Asp Tyr Ala His Ser Gln Arg Ala Leu Phe Asp Leu His Gln Arg Phe Ser Ser 755 Leu Lys Ala Val Leu Pro Pro Pro Ala Thr Gln Ala Pro Arg Thr Trp Leu His Tyr Tyr Arg Asn Trp Leu Gln Gly Ile Gln Ala Ala Phe Asp Gln Asp Trp Ala Ser Gly Arg Ile Thr Arg His Ser Tyr Arg Asn Gly Ser Glu Asp Gly Ala Leu Ala Tyr Lys Leu Leu Ile 815 Gln Thr Gly Asp Ala Gln Glu Pro Leu Asp Phe Ser Gln Leu Thr 835 Thr Arg Lys Leu Val Asp Arg Glu Gly Leu Ile Pro Pro Glu Leu 845 Phe Tyr Met Gly Leu Thr Val Trp Val Ser Ser Asp Pro Leu Gly Leu Ala Ala Ser Gln Ala Asn Phe Tyr Pro Pro Pro Pro Glu Trp

				875	5				880	)				885
Leu	His	s Asp	o Lys	Туг 890		o Thi	r Thi	r Gly	7 Glu 895		ı Let	ı Arç	] Ile	Pro 900
Pro	Ala	a Glr	n Pro	Leu 905		ı Phe	e Ala	a Gln	Phe 910		Phe	Leu	ı Leu	Arg 915
Gly	Leu	ı Glr	n Lys	Thr 920		a Asp	o Ph∈	e Val	Glu 925		Ile	e Glu	Gly	Ala 930
Arg	Ala	Ala	a Cys	Ala 935		a Ala	a Gly	/ Gln	Ala 940	Gly	Val	. His	Ala	Tyr 945
Pro	Ser	Gly	/ Ser	Pro 950		e Leu	Phe	Trp	Glu 955	Gln	Tyr	Leu	Gly	Leu 960
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Ala	Ala	His		Leu .055	Glu	His	Thr		Ala .060	Pro	Val	Thr	Asp 1	Gly 065
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Phe	Asp	Phe		Val .085	Arg	Tyr	Phe		Ala 090	Ala	Leu	Thr	Val 1	Leu 095
Thr	Leu	Leu		Leu 100	Leu	His	Gly		Val 105	Leu	Leu	Pro	Val 1	Leu 110
Leu	Ser	Ile		Gly 115	Pro	Pro	Pro		Val 120	Ile	Gln	Met	Tyr 1	Lys 125
Glu	Ser	Pro		Ile 130	Leu	Ser	Pro		Ala 135	Pro	Gln	Gly	Gly (	Gly L40
Leu	Arg	Trp		Ala 145	Ser	Ser	Ser		Pro 150	Gln	Ser	Phe	Ala A	Arg 155
Val	Thr	Thr		Met 160	Thr	Val	Ala		His 165	Pro	Pro	Pro	Leu E 11	Pro .70
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- Asp Arg Asp Tyr Leu His Arg Pro Ser Tyr Cys Asp Ala Ala Phe 50 55 60
- Ala Leu Glu Gln Ile Ser Lys Gly Lys Ala Thr Gly Arg Lys Ala
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- Pro Leu Trp Leu Arg Ala Lys Phe Gln Arg Leu Leu Phe Lys Leu 80 85 90
- Gly Cys Tyr Ile Gln Lys Asn Cys Gly Lys Ala Met Phe Asn Pro  $95 \hspace{1cm} 100 \hspace{1cm} 105 \hspace{1cm}$
- Gln Leu Met Ile Gln Thr Pro Lys Glu Glu Gly Ala Asn Val Leu 110 115 120
- Thr Thr Glu Ala Leu Leu Gln His Leu Asp Ser Ala Leu Gln Ala 125 130 135
- Ser Arg Val His Val Tyr Met Tyr Asn Arg Gln Trp Lys Leu Glu 140 145 150
- His Leu Cys Tyr Lys Ser Gly Glu Leu Ile Thr Glu Thr Gly Tyr 155 160 165
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- Pro Leu Asp Cys Phe Trp Glu Gly Ala Lys Leu Gln Ser Gly Thr 185 190 195
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505

500

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Ser Asp Trp Glu Thr Gly Lys Ile Met Pro Asn Asn Tyr Lys Asn 815 820 Gly Ser Asp Asp Gly Val Leu Ala Tyr Lys Leu Leu Val Gln Thr 830 Gly Ser Arg Asp Lys Pro Ile Asp Ile Ser Gln Leu Thr Lys Gln Arg Leu Val Asp Ala Asp Gly Ile Ile Asn Pro Ser Ala Phe Tyr 865 Ile Tyr Leu Thr Ala Trp Val Ser Asn Asp Pro Val Ala Tyr Ala 875 Ala Ser Gln Ala Asn Ile Arg Pro His Arg Pro Glu Trp Val His 890 895 Asp Lys Ala Asp Tyr Met Pro Glu Thr Arg Leu Arg Ile Pro Ala 905 910 Ala Glu Pro Ile Glu Tyr Ala Gln Phe Pro Phe Tyr Leu Asn Gly 920 925 Leu Arg Asp Thr Ser Asp Phe Val Glu Ala Ile Glu Lys Val Arg 935 940 Thr Ile Cys Ser Asn Tyr Thr Ser Leu Gly Leu Ser Ser Tyr Pro 950 Asn Gly Tyr Pro Phe Leu Phe Trp Glu Gln Tyr Ile Gly Leu Arg 965 His Trp Leu Leu Phe Ile Ser Val Val Leu Ala Cys Thr Phe 985 Leu Val Cys Ala Val Phe Leu Leu Asn Pro Trp Thr Ala Gly Ile 995 1000 Ile Val Met Val Leu Ala Leu Met Thr Val Glu Leu Phe Gly Met 1010 1015 Met Gly Leu Ile Gly Ile Lys Leu Ser Ala Val Pro Val Val Ile 1025 1030 Leu Ile Ala Ser Val Gly Ile Gly Val Glu Phe Thr Val His Val 1045 Ala Leu Ala Phe Leu Thr Ala Ile Gly Asp Lys Asn Arg Arg Ala 1055 1065 Val Leu Ala Leu Glu His Met Phe Ala Pro Val Leu Asp Gly Ala 1070 1075 Val Ser Thr Leu Leu Gly Val Leu Met Leu Ala Gly Ser Glu Phe 1085 Asp Phe Ile Val Arg Tyr Phe Phe Ala Val Leu Ala Ile Leu Thr Ile Leu Gly Val Leu Asn Gly Leu Val Leu Pro Val Leu Leu

1115 1120 1125

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Asn Arg Leu Pro Thr Pro Ser Pro Glu Pro Pro Pro Ser Val Val 1145 1150 1155

Arg Phe Ala Met Pro Pro Gly His Thr His Ser Gly Ser Asp Ser 1160 1165 1170

Ser Asp Ser Glu Tyr Ser Ser Gln Thr Thr Val Ser Gly Leu Ser 1175 1180 1185

Glu Glu Leu Arg His Tyr Glu Ala Gl<br/>n Gln Gly Ala Gly Gly Pro\$1190\$1195 1200

Ala His Gln Val Ile Val Glu Ala Thr Glu Asn Pro Val Phe Ala 1205 1210 1215

His Ser Thr Val Val His Pro Glu Ser Arg His His Pro Pro Ser 1220 1225 1230

Asn Pro Arg Gln Gln Pro His Leu Asp Ser Gly Ser Leu Pro Pro 1235 1240 1245

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Leu Trp Pro Pro Leu Tyr Arg Pro Arg Arg Asp Ala Phe Glu Ile 1265 1270 1275

Ser Thr Glu Gly His Ser Gly Pro Ser Asn Arg Ala Arg Trp Gly 1280 1285

Pro Arg Gly Ala Arg Ser His Asn Pro Arg Asn Pro Ala Ser Thr 1295 1300 1305

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1340 1345 1350

Tyr Pro Glu Thr Asp His Gly Leu Phe Glu Asp Pro His Val Pro 1355 1360 1365

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Ser Asn

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275

Phe Ser His Lys Phe Met His Trp Gln Glu Glu Leu Leu Gly 290 295 Gly Thr Ala Arg Asp Leu Gln Gly Gln Leu Leu Arg Ala Glu Ala 305 Leu Gln Ser Thr Phe Leu Leu Met Ser Pro Arg Gln Leu Tyr Glu 320 His Phe Arg Gly Asp Tyr Gln Thr His Asp Ile Gly Trp Ser Glu Glu Gln Ala Ser Met Val Leu Gln Ala Trp Gln Arg Arg Phe Val 350 Gln Leu Ala Gln Glu Ala Leu Pro Ala Asn Ala Ser Gln Gln Ile 370 His Ala Phe Ser Ser Thr Thr Leu Asp Asp Ile Leu Arg Ala Phe 380 385 Ser Glu Val Ser Thr Thr Arg Val Val Gly Gly Tyr Leu Leu Met 395 Leu Ala Tyr Ala Cys Val Thr Met Leu Arg Trp Asp Cys Ala Gln 415 Ser Gln Gly Ala Val Gly Leu Ala Gly Val Leu Leu Val Ala Leu 430 Ala Val Ala Ser Gly Leu Gly Leu Cys Ala Leu Leu Gly Ile Thr Phe Asn Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu Gly 460 Ile Gly Val Asp Asp Ile Phe Leu Leu Ala His Ala Phe Thr Lys 475 Ala Pro Pro Asp Thr Pro Leu Pro Glu Arg Met Gly Glu Cys Leu 485 490 Arg Ser Thr Gly Thr Ser Val Ala Leu Thr Ser Val Asn Asn Met Val Ala Phe Phe Met Ala Ala Leu Val Pro Ile Pro Ala Leu Arg 515 520 Ala Phe Ser Leu Gln Ala Ala Ile Val Val Gly Cys Asn Phe Ala 530 Ala Val Met Leu Val Phe Pro Ala Ile Leu Ser Leu Asp Leu Arg Arg Arg His Arg Gln Arg Leu Asp Val Leu Cys Cys Phe Ser Ser Pro Cys Ser Ala Gln Val Ile Gln Met Leu Pro Gln Glu Leu Gly Asp Arg Ala Val Pro Val Gly Ile Ala His Leu Thr Ala Thr Val

	•			590					595					600		-	
Gln	Ala	Phe	Thr	His 605	Cys	Glu	Ala	Ser	Ser 610		His	Val	Val	Thr 615			
Ile	Leu	Pro	Pro	Gln 620	Ala	His	Leu -	Leu	Ser 625		Ala	Ser	Asp	Pro 630			•
Leu	Gly	Ser	Glu	Leu 635	Tyr	Ser	Pro	Gly	Gly 640	Ser	Thr	Arg	Asp	Leu 645			
Leu	Ser	Gln	Glu	Glu 650	Gly	Thr	Gly	Pro	Gln 655	Ala	Ala	Cys	Arg	Pro 660			
Leu	Leu	Cys	Ala	His 665	Trp	Thr	Leu	Ala	His 670	Phe	Ala	Arg	Tyr	Gln 675			1
Phe	Ala	Pro	Leu	Leu 680	Leu	Gln	Thr	Arg	Ala 685	Lys	Ala	Leu	Val	Leu 690			
Leu	Phe	Phe	Gly	Ala 695	Lęu	Leu	Gly	Leu	Ser 700	Leu	Tyr	Gly	Ala	Thr 705			
Leu	Val	Gln	Asp	Gly 710	Leu	Ala	Leu	Thr	Asp 715	Val	Val	Pro	Arg	Gly 720			
Thr	Lys	Glu	His	Ala 725	Phe	Leu	Ser	Ala	Gln 730	Leu	Arg	Tyr	Phe	Ser 735			
Leu	Tyr	Glu	Val	Ala 740	Leu	Val	Thr	Gln	Gly 745	Gly	Phe	Asp	Tyr	Ala 750			
His	Ser	Gln	Arg	Ala 755	Leu	Phe	Asp	Leu	His 760	Gln	Arg	Phe	Ser	Ser 765			
Leu	Lys	Ala	Val	Leu 770	Pro	Pro	Pro	Ala	Thr 775	Gln	Ala	Pro	Arg	Thr 780			
Trp	Leu	His	Tyr	Tyr 785	Arg	Ser	Trp	Leu	Gln 790	Gly	Ile	Gln	Ala	Ala 795			
Phe	Asp	Gln	Asp	Trp 800	Ala	Ser	Gly	Arg	Ile 805	Thr	Cys	His	Ser	Tyr 810			
Arg	Asn	Gly	Ser	Glu 815	Asp	Gly	Ala	Leu	Ala 820	Tyr	Lys	Leu	Leu	11e 825	 		
Gln	Thr	Gly	Asn	Ala 830	Gln	Glu	Pro	Leu	Asp 835	Phe	Ser	Gln	Leu	Thr 840			
Thr	Arg	Lys	Leu	Val 845	Asp	Lys	Glu	Gly	Leu 850	Ile	Pro	Pro		Leu 855			
Phe	Tyr	Met	Gly	Leu 860	Thr	Val	Trp	Val	Ser 865	Ser	Asp	Pro		Gly 870			
Leu	Ala	Ala		Gln 875	Ala	Asn	Phe	Tyr	Pro 880	Pro	Pro	Pro		Trp 885			
Leu	His	Asp		Tyr 890	Asp	Thr	Thr		Glu 895	Asn	Leu	Arg		Pro 900			

Ala Ala Gln Pro Leu Glu Phe Ala Gln Phe Pro Phe Leu Leu His 905 910 915

Gly Leu Gln Lys Thr Ala Asp Phe Val Glu Ala Ile Glu Gly Ala 920 925 930

Arg Ala Ala Cys Thr Glu Ala Gly Gln Ala Gly Val His Ala Tyr 935 940 945

Pro Ser Gly Ser Pro Phe Leu Phe Trp Glu Gln Tyr Leu Gly Leu 950 955 960

Arg Arg Cys Phe Leu Leu Ala Val Cys Ile Leu Leu Val Cys Thr 965 970 975

Phe Leu Val Cys Ala Leu Leu Leu Ser Pro Trp Thr Ala Gly 980 985 985

Leu Ile Val Leu Val Leu Ala Met Met Thr Val Glu Leu Phe Gly
995 1000 1005

Ile Met Gly Phe Leu Gly Ile Lys Leu Ser Ala Ile Pro Val Val 1010 1015 1020

Ile Leu Val Ala Ser Ile Gly Ile Gly Val Glu Phe Thr Val His 1025 1030 1035

Val Ala Leu Gly Phe Leu Thr Ser His Gly Ser Arg Asn Leu Arg 1040 1045 1050

Ala Ala Ser Ala Leu Glu Gln Thr Phe Ala Pro Val Thr Asp Gly 1055 1060 1065

Ala Val Ser Thr Leu Leu Gly Leu Leu Met Leu Ala Gly Ser Asn 1070 1075 1080

Phe Asp Phe Ile Ile Arg Tyr Phe Phe Val Val Leu Thr Val Leu . 1085 1090 1095

Thr Leu Leu Gly Leu Leu His Gly Leu Leu Leu Pro Val Leu 1100 1105 1110

Leu Ser Ile Leu Gly Pro Pro Pro Gln Val Val Gln Val Tyr Lys 1115 1120 1125

Glu Ser Pro Gln Thr Leu Asn Ser Ala Ala Pro Gln Arg Gly Gly
1130 1135 1140

Leu Arg Trp Asp Arg Pro Pro Thr Leu Pro Gln Ser Phe Ala Arg 1145 1150 1155

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ttacaccaag gagaagctgg gggaggaggc tgcatacacc tctcagatgc 350 tgatacagac cgcacgccag gagggagaga acatecteae acecgaagea 400 cttggcctcc acctccaggc agccctcact gccagtaaag tccaagtatc 450 actctatggg aagtcctggg atttgaacaa aatctgctac aagtcaggag 500 ttccccttat tgaaaatgga atgattgagt ggatgattga gaagctgttt 550 ccgtgcgtga tcctcacccc cctcgactgc ttctgggagg gagccaaact 600 ccaagggggc tecgeetace tgeeeggeeg eeeggatate eagtggaeea 650 acctggatee agageagetg etggaggage tgggteeett tgeeteeett 700 gagggettee gggagetget agacaaggea caggtgggee aggeetaegt 750 ggggcggccc tgtctgcacc ctgatgacct ccactgccca cctagtgccc 800 ccaaccatca cagcaggcag gctcccaatg tggctcacga gctgagtqqq 850 ggctgccatg gcttctccca caaattcatg cactggcagg aggaattgct 900 gctgggaggc atggccagag acccccaagg agagctgctg agggcagagg 950 ccctgcagag caccttcttg ctgatgagtc cccgccagct gtacgagcat 1000 ttccggggtg actatcagac acatgacatt ggctggagtg aggagcaggc 1050 cagcacagtg ctacaagcct ggcagcggcg ctttgtgcag ctggcccagg 1100 aggccctgcc tgagaacgct tcccagcaga tccatgcctt ctcctccacc 1150 accetggata acateetgea tgegttetet gaagteagtg etgeeegtgt 1200 ggtgggaggc tatctgctca tgctggccta tgcctgtgtg accatgctgc 1250 ggtgggactg cgcccagtcc cagggttccg tgggccttgc cggggtactg 1300 ctggtggccc tggcggtggc ctcaggcctt gggctctgtg ccctgctcgg 1350 catcacette aatgetgeea etacecaggt getgeeette ttggetetgg 1400 gaatcggcgt ggatgacgta ttcctgctgg cgcatgcctt cacagaggct 1450 ctgcctggca cccctctcca ggagcgcatg ggcgagtgtc tgcagcgcac 1500 gggcaccagt gtcgtactca catccatcaa caacatggcc gccttcctca 1550 tggctgccct cgttcccatc cctgcgctgc gagccttctc cttacagcca 1600 tecteageet ggacetaegg eggegeeact geeagegeet tgatgtgete 1650 tgctgcttct ccagtccctg ctctgctcag gtgattcaga tcctgcccca 1700 ggagetgggg gaegggaeag taccagtggg cattgeecae etcaetgeea 1750 cagttcaagc ctttacccac tgtgaagcca gcagccagca tgtggtcacc 1800 atcctgcctc cccaagccca cctggtgccc ccaccttctg acccactggg 1850

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GITIAITITCAG GCCATGGIGI TGCGCCGAAT TAATTCCCGA TCCAGACATG ATAAGATACA TIGATGAGTT TGGACAAACC ACAACTAGAA TGCAGTGAAA CAATAAAGIC CGGTACCACA ACGCGGCTTA ATTAAGGGCT AGGTCTGTAC TATTCTATGT AACTACTCAA ACCTGTTTGG TGTTGATCTT ACGTCACTTT

CCGCAGCACC TUGACTICTAG AGGATICICICG GGGAATTICG GCATGACTICG ATGGCGCCCC CTCAGAGAGC TGCCCCCGAG TTACACACCC CCAGCTCGAA TAGCGGCGGG GAGTCTCTCG ACGGGGCTC AATGTGTGGG GGTCGAGCTT Д . [2] œ Д Д ß AGCTGAGATC TCCTAGGGGC CCCTTAAGGC CGTACTGAGC 201

CGIGCTIACT ICCAGGCCT GCICTICTCT CTGGGAIGCG GGAICCAGAG ACATIGIGGC TGTAACACCG ပ GCACGAATGA AGGICCCGGA CGAGAAGAGA GACCCIACGC CCIAGGICTC a Н G ပ ဗ ᆸ ഗ ᆸ H G Ø > Ø ACTCTGGCTT TGAGACCGAA 3 ᆸ TGAAGGCTCC ACTTCCGAGG æ CGACCCTCGG GCTGGGAGCC ഗ GCTCTAGGAT CCAGATCCTA H 301

GTAGAAGTGG CATCTTCACC > Œ GITGGCCTTT GGGGCCCTGG CATTAGGTCT CCGCATGGCC ATTATTGAGA CAAACTTGGA ACAGCTCTGG TGTCGAGACC ᆸ O GTAATCCAGA GGCGTACCGG TAATAACTCT GTTTGAACCT H z ы Ψ Ψ 2 ы တ ,... TTTCACGAGA AAGACCCTGA CAACCGGAAA CCCCGGGACC ᆸ æ ပ [L K ы TTCTGGGACT ဗ ... AAAGTGCTCT L > × 401 57

GAGGCTGCAT ACACCTCTCA GATGCTGATA CAGACCGCAC GCCAGGAGGG TGTGGAGAGT CTACGACTAT GTCTGGCGTG CGGTCCTCCC Æ; ۴ Н u ¥. O ഗ ۲ CTCCGACGTA æ Æ, ы GCTGGGGGAG CGACCCCCTC G ပ Ä GACGTAATGT GGTTCCTCTT GAGCCAGGAG CTGCATTACA CCAAGGAGAA EП × × × CTCGGTCCTC (L) S 501 GCAGCCGGGT CGTCGGCCCA 91

CTGGGATTTG GACCCTAAAC 3 CTCACACCCG AAGCACTTGG CCTCCACCTC CAGGCAGCCC TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC CATAGTGAGA TACCCTTCAG × လ GGAGGTGGAG GTCCGTCGGG AGTGACGGTC ATTTCAGGTT > × æ H J æ æ H H GAGTGTGGC TTCGTGAACC ပ J æ 四 പ AGAGAACATC TCTCTTGTAG 601 124

TGTTTCCGTG CGTGATCCTC ACCCCCTCG GCACTAGGAG TGGGGGGAGC J H > TACCTTACTA ACTCACCTAC TAACTCTTCG ACAAAGGCAC 701 AACAAAATCT GCTACAAGTC AGGAGTTCCC CTTATTGAAA ATGGAATGAT TGAGTGGATG ATTGAGAAGC × 回 Σ ы Z G GAATAACTTT Œ TCCTCAAGGG > ပ CGATGTTCAG > TTGTTTTAGA z 157

FIG.\_ 1A

GAGTGAGGAG CAGGCCAGCA CAGTGCTACA AGCCTGGCAG

GTCACGATGT

CTCACTCCTC GTCCGGTCGT

TGTAACCGAC

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GCACCCTGAT

ATGCACCCCG CCGGGACAGA

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CCCTTGAGGG CTTCCGGGAG CTGCTAGACA AGGCACGGT GGGCCAGGCC TACGTGGGGC GGCCCTGTCT

TCCGTGTCCA

GGGAACTCCC GAAGGCCCTC GACGATCTGT

CTAGGTCTCG

CTGGTTGGAC

CCGCCGGCC TATAGGTCAC

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801 ACTGCTTCTG TGACGAAGAC

GGAGGGAGCC AAACTCCAAG GGGGCTCCGC CTACCTGCCC GGCCGCCCGG ATATCCAGTG GACCAACCTG GATCCAGAGC

GATGGACGGG

CCCCGAGGCG

TTTGAGGTTC

TCCCACAAAT

CCATGGCTTC

CACGAGCTGA GTGGGGGCTG

GTAGTGTCGT CCGTCCGAGG GTTACACCGA

GACCTCCACT GCCCACCTAG TGCCCCCAAC CATCACAGCA GGCAGGCTCC CAATGTGGCT

CTGGAGGTGA CGGGTGGATC ACGGGGGTTG

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CCCTTTGCCT GGGAAACGGA

GGAGCTGGGT CCTCGACCCA

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CAGAGACCCC CAAGGAGAGC TGCTGAGGGC AGAGGCCCTG CAGAGCACCT TCTTGCTGAT

GTTCCTCTCG ACGACTCCCG

CICCGIACCG GICTCIGGGG

TTGCTGCTGG GAGGCATGGC

GCAGGAGGAA

TCATGCACTG AGTACGTGAC

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CGTCCTCCTT AACGACGACC

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GGGTGACTAT CAGACACATG ACATTGGCTG

CAGCTGTACG AGCATTTCCG

GAGTCCCCGC CTCAGGGGCG

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TCGTAAAGGC

GTCGACATGC

CCCACTGATA GTCTGTGTAC

TGCCACTACC GAGCCGTAGT GGAAGTTACG CTGTGCCCTG CTCGGCATCA CCTTCAATGC ტ GACACGGGAC GAACGGCCCC ATGACGACCA CCGGGACCGC CACCGGAGTC CGGAACCCGA u ဗ Ġ လ Ø 'A L ပ AAGCCACCCG 424

AGTCCCAGGG CACACTGGTA CGACGCCACC CTGACGCGGG 3 α, ᆸ E > CGAGTACGAC CGGATACGGA ပ æ A Z Z ᆸ CTCCGATAGA ဟ GCACACCACC > α GTCACGACGG ഗ AGAGACTTCA Ħ 391

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CTGCATGCGT CCTACTGTAG GCAGATCCAT GCCTTCTCT CCACCACCCT GGATGACATC GGTGGTGGGA CGGAAGAGGA CGTCTAGGTA GCCGCGAAAC ACGTCGACCG GGTCCTCCGG GACGGACTCT TGCGAAGGGT ᆸ 357

CGGCGCTTTG TGCAGCTGGC CCAGGAGGCC CTGCCTGAGA ACGCTTCCCA 臼 Ø 1301

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GCCTATGCCT GTGTGACCAT GCTGCGGTGG GACTGCGCCC GCTCATGCTG TCTCTGAAGT CAGTGCTGCC CGTGTGGTGG GAGGCTATCT

GGCCCTGGCG GTGGCCTCAG GCCTTGGGCT CTTGCCGGGG TACTGCTGGT TTCCGTGGGC 1501

	:	30	40	50	60	. 70
905531	GCI	GGGGTGCAC	GCCTACCNCA	GCGGNTCCCC	°C™™CC™C™™	70
	•	• • • • • • •	***	***	*****	معاملة بالأناف
hpatched	d CTG	GGGCTGTCC	AGTTACCCCA	ACGGCTACCC	СТТССТСТТС	TCCCACCA
* * * * * * * *	3010	3020	3030	3040	3050	
	•.					
. 005531	-	80	90	100	110	120
905531	GTA	TCTGGGCCT	GCGGCGCTGC	PTCCTGCTGG	CCGTCTGCAT	СТСТССТСС
	** ** **		** ***	* ****	* ** ** *	
hpatched	GTA	CATCGGCCT	CCGCCACTGG	TGCTGCTGTT	CATCAGCGTG	CTCTTCC
	3060	3070	3080	3090	3100	.G1G11GG
005504		130	140	150	160	170
905531	TGT	<b>SCACTTTCC</b>	CGTCTGTGCT	CTGCTGCTCC	TNAACCCCTC	C)CCCC
•			**** ** ***	* * **	*****	
hpatched		CACATTCCT	CGTGTGCGCT	GTCTTCCTTC	ጥር እ እ ር ር ር ር ጥር	CACCCCC
,	3110	3120	3130	3140	3150	GACGGCC
<b>.</b>		180	190	200	210	220
905531	GGCC	TNATAGTGC	TGGTCCTGGC	GATGATGACA	GTGGAACTCT	TGG†AT
hpatched	GGGA				** ** ** *	* ** **
_	3160	3170	TGGTCCTGGC	CTGATGACG(	GTCGAGCTGTI	CGGCAT
. ·	7100	31/0	3180	3190	3200	
005537		230	240	250		
905531	CATG	GGTTTNCTG	ggcátcaagci	GAGT		
1	***	** ** * 1	** *****	***		
hpatched	GATG	GCCTCATC	GAATCAAGCT	CAGT		
3	210	3220	3230		•	
		••		•		

905531	80 TCTGGGCCTGC	90 360607607	100	110	120
hpatched	::: ::: GCTGCTGCTGT 3090	* **	*    **  **** TGGTGTTGGCC	**** TGCACA	* ** ***
905531	130 GCACTTTCCTC	140 TCTGTGCT	150 CTGCTGCT		
hpatched	GCGCTGTCTTCC		: : CCCTGGAC	. ·	

## 7/29

GCTGGGGTGCACGCCTACCCCAGCGGCTCCCCCTTCCTCTTCTGGGAACA CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTCTGGGAGCA hpatched GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG hpatched GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTCATCAGCGTGGTGTTGG TGTGCACTTTCCTCNTCTGTGCTCT hpatched CCTGCACATTCCTCGTGTGCGCTGT 

TCTGGGCCTGCGGCGCTCTCCTGCTGCTCTCCTGCTGTGT  ${\tt GCTGCTGCTGTTCATCAGCGTGTGTTGGCC---TGCACATTCCTCGTGT}$ hpatched GCACTTTCCTCNTCTGTGCTCT hpatched GCGCTGTCTTCCTGAACCC 

10 20 30 40 50
CCGGGCAGCATGCGCAGAGGCCGGCCAGGCTGGGGTGCACGCCTACCCCA

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hpatched.RC
CCGGGCGGCATG--GCGAAGCGGACCACGCTGGGGGGTGGCTCAGGGGAG
710 720 730 740 750

Œ A G PODRGGGGGCIGAPGR PTCH2 PTCH

LLFIKILGOVIOKNICG H R P S Y C D A A F A L E Q I S K G K A T G R K A P L W L R A K F Q R L I - P P S Y T P P - - A R T A A P Q I L A G S L K A P L W L R A Y F Q G L I 12 PTCH2

LWVEVGSRVSOELHYTKEK ETNVEELWVEVGGRVSRELN PTCH2

TEALLOHLDSALOASRVHVYMYNROWKLE PEALGLHLOAALTASKVOVSLYGKSWDLN 151 108 PTCH2

TPLDCFWEGAKLQSGTAYI TPLDCFWEGAKLQGGSAY 201 HLCYKSGELITETGYMDQIIEYL 158 KICYKSGVPLIENGMIEWMIEKL PTCH2

LEELKKINYQVDSWEEMLNKAEVGHGYMDRPCL LEELGPFA-SLEGFRELLDKAQVGQAYVGRPCL 251 KPPLRWINFOPLEF 208

301 DPDCPATAPNKNSTKPLDMALVLNGGCHGLSRKYMHWQEELIVGGTVKN 257 DLHCPPSAPNHHSRQAPNVAHELSGGCHGFSHKFMHWQEELLLGGMARD PTCH PTCH2

LMTPKOMYEHFKGYEYVSH.INWNEDKAAA LMSPROLYEHFRG.DYQTHDIGWSEEQAST 400 GRTYVEVVHQSVAQNSTOKVLSFTTTTLDD1 PTCH2 PTCH2

TMIRWDCA OSOGSVGLAGW 406

456

O A A PALRAFSL PTCH2

600 LYRREDRRLDIFCCFTSPCVSRVIQVEPOAYTOTHONTRYSPPPYSSH 554 LRRRHCORLDVLCCFSSPCSAOVIQILPOELGOGT.....VPV PTC<sub>72</sub> PTCH

650 FAHET 593 PTCH PTCH2

700 OSPESTSSTRDLLSOFSDSSLH..GLEPPGTKWT 634 ELFSPGGSTRDLLGOEEETROKAACKSLPCARWN PTCH PTCH2

V P R E T R E Y D F I V P R G T K E H A F L 684 PTCH2

V T O K A . D Y P N I O H L L Y D L H R S F S N V K Y I V T O G G F D Y A H S O R A L F D L H O R F S S L K A L 3 F S F Y N M Y 1 N

AYKLLVQTGSRDKP AYKLLIQTGDAQEP ODAFDSDWETGKIMPNNYKNGSDDGVLAYKLLVOAAFDODWASGRITRHSYRNGSEDGALAYKLLI YFRDWLOGLO PTCH2

INPSAFY IYL TAWVSNOPVAYAASQAN I RPHRP IPPELFYMGL TVWVSSDPLGLAASQANFYPPP PTCH2

L NG L R D T S D F V E A I E K V R T L R G L O K T A D F V E A I E G A R A EWVHDKADYMPETRLRIPAAEPIEYAQFPFYIEWLHDKYD-TTGENLRIPPAOPLEFAOFPFL PTCH2

GL RHV 997 I CSNYTSLGLSSYPNGYPFLFWEQY 933 A CAEAGOAGVHAYPSGSPFLFWEQY PTCH PTCH2

VHVALJAFLTA IGDKINRIRAVLIALEH PTCH2 1033 🖹 V H V A L G F L T T 이 G S R IN L IR A A H A L E H 1097

NGLVLLPVLLSFFGPYPEVSPANGLNRLP HGLVLLPVLLSILGPPPEVIOMYKESPEI FIVRYFFA PTCH2 1083 F 1 V R Y F F A

PTCH 1197 SPEPPPSVVRFAMPPGHTHSGSDSSDSEYSSOTTVSGLSEELRHYEAQO1 PTCH2 1133 PPAPQGGGLRWGASSSLPQS-FARVTTSMTVAIHPPPLPGAYIHPAPDEI

PPSNPRQQPHLD SRHHE 1247 A G G PA HOVIVE A TENP V F A H S T V V H P E PTCH2 1182 PWSPAATSSGNLSSRGPGPAT

EGHSGPSNRARWGPR PRRDAFEIST REGLWPPLYR 1297 R Q G Q Q P R R D P P 쬬

P A S T A M G S S V P G Y C Q P I T T V T A S A S V T V A V H P P P V P G P G R N P R 1347 H N P R N PTGH

1397 L C P G Y P E T D H G L F E D P H V P F H V R C E R R D S K V E V I E L Q D V E C E PTCH

G.\_3D PTCH 1447 N

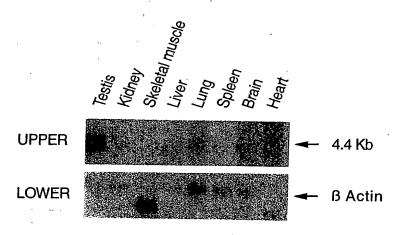
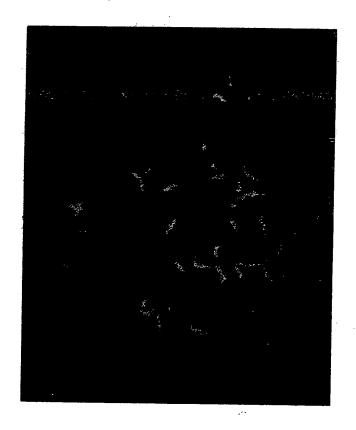
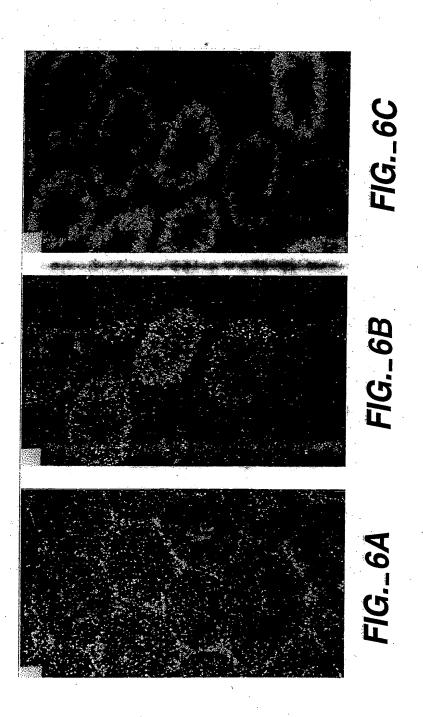
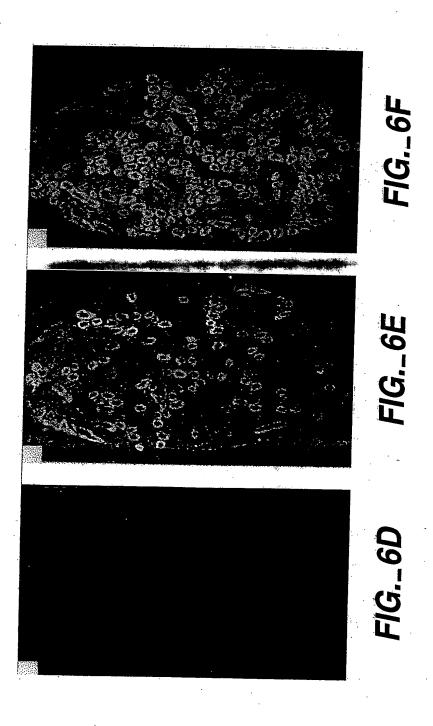


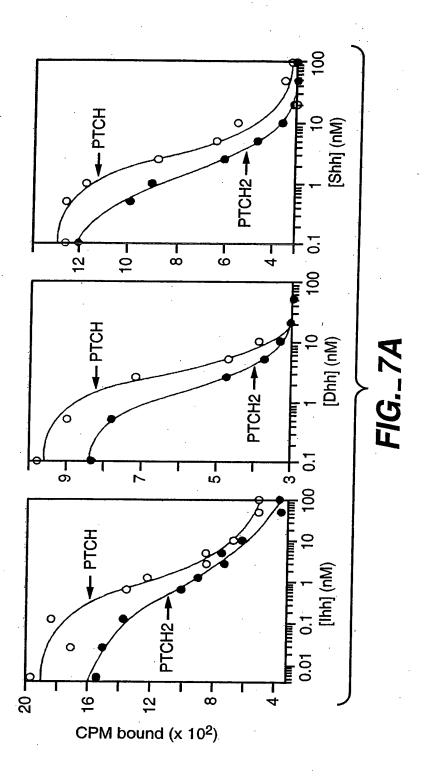
FIG.\_4

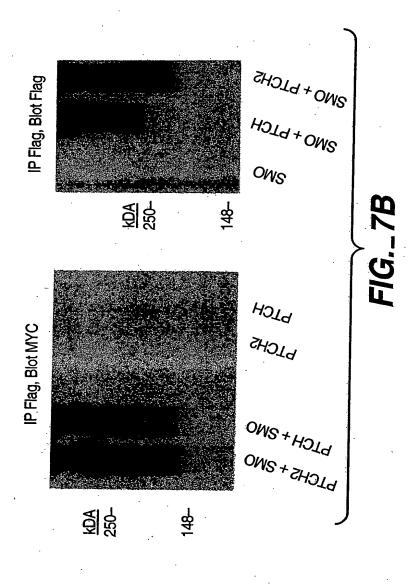


**FIG.\_5** 









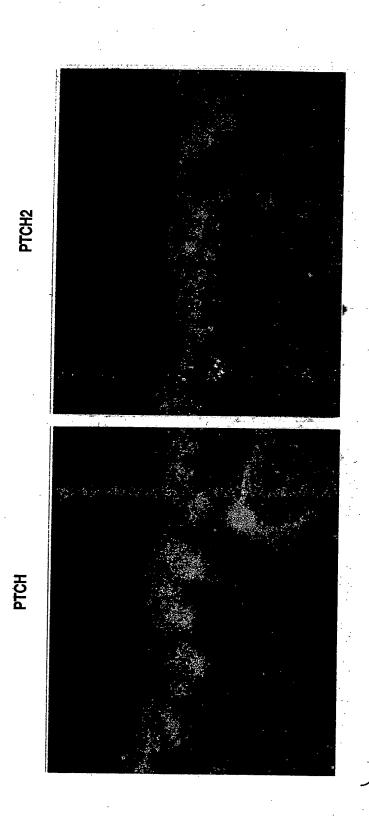
Docket No.: P1405R1C1

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	10	20	30	40	- 50
h <i>Ptch</i> -2	MTRSPPLRELPPS	SYTPPARTAAP	QILAGSLKA	LWLRAYFOGL	LFSLGCG
	* * . * ****	*****	*****	*****	t.***
mPatched:	2 MVRPLSLGELPPS	YTPPARSSAP	HILAGSLOAE	LWLRAYFOGLI	FSLGCR
	10	20	30	40	50 50
	•				50
	60	70	80	90	100
h <i>Ptch</i> -2	IQRHCGKVLFLGL				
	**.*******	*****	*.*.***.**	******	*****
mPatched2	1QKHCGKVLFLGL				
	60	70	80	90	100
	110	120	. 130	140	150
h <i>Ptch</i> -2	KEKLGEEAAYTSQ	MLIQTARQEGE	ENILTPEALG		
	********	*****	*:*****	******	*****
mPatched2	KEKLGEEAAYTSQ				
	. 110	120	130	140	150
	160	170	180	190	200
h <i>Ptch</i> -2	GKSWDLNKICYKS	GVPLIENGMIE	WMIEKLFPC	VILTPLDCFWE	GAKLQG
	*****	*****	.*****	******	****
mPatched2	GKSWDLNKICYKS	GVPLIENGMIE	RMIEKLFPC	VILTPLDCFWE	GAKLQG
	160	170	180	190	200
	210	220	230	240	250
h <i>Ptch</i> -2	GSAYLPGRPDIQWY	NLDPEQLLEE	LGPFASLEGE	RELLDKAQVG	<b>QAYVGR</b>
<b></b>	*****				
mPatched2	GSAYLPGRPDIQWI				<b>QAYVGR</b>
-	210	220	230	240	250
	260	270	280	290	300
h <i>Ptch</i> -2	PCLHPDDLHCPPSA	PNHHSRQAPN	VAHELSGGCH	IGFSHKFMHWQE	ELLLG
·	***.*** *****				
mPatched2	PCLDPDDPHCPPSA			IGFSHKFMHWQE	ELLLG
·	260	270	280	290	300
	310	320	330	340	350
h <i>Ptch</i> -2	GMARDPQGELLRAE	ALQSTFLLMS	PRQLYEHFRG	DYQTHDIGWSE	EQAST
_	* *** ** ****				
mPatched2	GTARDLQGQLLRAE		PRQLYEHFRG	DYQTHDIGWSE	EQASM
	310	320	330	340	350

FIG.\_8A

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 $FIG._{9}$ 

101 GCACTTGGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAAGTCCT GGGATTTGAA CAAAATCTGC TACAAGTCAG CGTGAACCGG AGGTGGAGGT CCGTCGGGAG TGACGGTCAT TTCAGGTTCA TAGTGAGATA CCCTTCAGGA CCCTAAACTT GTTTTAGACG ATGITCAGTC 1 CCCACGCGTC CGGGAGAAGC TGGGGGAGGA GGCTGCATAC ACCTCTCAGA TGCTGATACA GACGGCACGC CAGGAGGGAG AGAACATCCT CACACCCGAA GGGTGCGCAG GCCCTCTTCG ACCCCCTCCT CCGACGTATG TGGAGAGTCT ACGACTATGT CTGGCGTGCG GTCCTCCCTC TCTTGTAGGA GTGTGGGCTT

201 GAGTICCCCT TAITGAAAAI GGAATGATTG AGCGGATGAT TGAGAAGCTG TTTCCGTGCG TGAICCTCAC CCCCTCGAC TGCTTCTGGG AGGGAGCCAA CTCAAGGGGA ATAACTITITA CCTTACTAAC TCGCCTACTA ACTCTTCGAC AAAGGCACGC ACTAGGAGTG GGGGGAGCTG ACGAAGACCC TCCCTCGGTF 301 ACTCCAAGGG GGCTCCGCCT ACCTGCCGCT CCCAATGTGG CTCACGAGCT GAGTGGGGGC TGCCATGGCT TCTCCCACAA ATTCATGCAC TGGCAGGG TGAGGTTCCC CCGAGGCGGA TGGACGGCGA GGGTTACACC GAGTGCTCGA CTCACCCCCG ACGGTACCGA AGAGGGTGTT TAAGTACGTG ACCGTCCTCC 401 AATTGCTGCT GGGAGGCATG GCCAGAGACC CCCAAGGAGA GCTGCTGAGG GCAGAGGCCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCCC GCCAGCTGTA TTAACGACGA CCCTCCGTAC CGGTCTCTGG GGGTTCCTCT CGACGACTCC CGTCTCCGGG ACGTCTCGTG GAAGAACGAC TACTCAGGGG

501 CGAGCATTIC CGGGGTGACT ATCAGACACA TGACATTGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGGGGGCTT TGTGCAGGTC ACACGTCCAG TCGCCGCGAA GCTCGTAAAG GCCCCACTGA TAGTCTGTGT ACTGTAACCG ACCTCACTCC TCGTCCGGTC GTGTCACGAT GTTCGGACCG

GGTATGGACA AGGACAGGGG GGTGCCCTGA GGCCATTCCC TCCTCCTGCC CCCTCTATC CACCCTGTTT CTCCAGGTGG CCCAGGAGGC CCTGCCTGAG TCCTGTCCCC CCACGGGACT CCGGTAAGGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTCGACC GGGTCCTCCG GGACGGACTC

FIG.\_ 10A

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701 AACGCTTCCC AGCAGATCCA TGCCTTCTCC TCCACCACCC TGGATGACAT CCTGCATGCG TTCTCTGAAG TCAGTGCTGC CCGTGTGGTG GGAGGCTATC TTGCGAAGGG TCGTCTAGGT ACGGAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACGC AAGAGACTTC AGTCACGACG GGCACACCAC

ACGAGTACCA CCCAGAACGT GGACCGTGGA ACGGGGGTGG GGTGGAGGTT GGTCACGGGT GGGACCCCTC GGGGACTCTG ACGGGAAAGG GGGGTGTCGA 801 TGCTCATGGT GGGTCTTGCA CCTGGCACCT TGCCCCCACC CCACCTCCAA CCAGTGCCCA CCCTGGGGAG CCCCTGAGAC TGCCCTTTCC CCCACAGCT

901 GOCCTATGCC TGTGTGACCA TGCTGCGGTG GGACTGCGCC CAGTCCCAGG GTTCCGTGGG CCTTGCCGGG GTACTGCTGG TGGCCCTGGC GGTGGCCTCA CCGGATACGG ACACACTGGT ACGACGCCAC CCTGACGCGG GTCAGGGTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG CCACCGGAGT

COGGAACCO AGACACGGGA CGAGCCGTAG TGGAAGTTAC GACGGTGATG GGTCCATGCG GTCCTGACGT CCCGTCTGAG TCACGGTCAG TGGTCCGAAG 1001 GGCCTTGGGC TCTGTGCCCT GCTCGGCATC ACCTTCAATG CTGCCACTAC CCAGGTACGC CAGGACTGCA GGGCAGACTC AGTGCCAGTC ACCAGGCTTC

1101 ACGGGTCCTC AGCTGCCCGC TCCTCTGCCC CTCCAGGTGC TGCCCTTCTT GACTCTGGGA ATCGGCGTGG ATGACGTATT CCTGCTGGCG CATGCCTTCA TCGÁCGGGCG AGGAGACGGG GAGGTCCACG ACGGGAAGAA CTGAGACCCT TAGCCGCACC TACTGCATAA GGACGACCGC GCCCAGGAG

1201 CAGAGGCTCT GCCTGGCACC CCTCTCCAGG TGGGGCCTTG TCCCCCAGGG CTCATCTGAG GCAGCTCAGC TTACTGGTTA AGAGCCTCTT GGTTCAAGTG GTCTCCGAGA CGGACCGTGG GGAGAGGTCC ACCCCGGAAC AGGGGGTCCC GAGTAGACTC CGTCGAGTCG AATGACCAAT TCTCGGAGAA CCAAGTTCAC

1301 ACCTIGGGCT GCTAATGAAC CTCGGTGCCT CTTGTCCCCA TGTGTAAACA GGGGAATAA TAGTGCTGTG TCCTAAGGGT TATTGTTTGG ATCAGTGAAG CCCCTITAIT ATCAGACAC AGGATTCCCA ATAACAAACC TAGTCACTTC IGGAACCCGA CGATTACTTG GAGCCACGGA GAACAGGGGT ACACATTTGT

1401 TAACTCAAGT TGAATGCTTA GAACAGCCCA TCATACGTAC ATGGTACCCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCCAAGTT ATTGAGITICA ACTIACGAAT CITGICGGGI AGIATGCATG TACCATGGGI TATTTACGAT CGGTGACACA ATACTGACGG GGTGGAGACG TGGGGTTCAA

# FIG.\_ 10B

1601 CAGCGCACGG GCACCAGTGT TGTACTCACA TCCATCAACA ACATGGCCGC CTTCCTCATG GCTGCCCTCG TTCCCATCCC TGCGCTGCGA GCCTTCTCCC GTCGCGTGCC CGTGGTCACA ACATGAGTGT AGGTAGTTGT TGTACCGGCG GAAGGAGTAC CGACGGGAGC AAGGGTAGGG ACGCGACGCT CGGAAGAGGG 1701 TACAGCCTGG ACCTACGGCG GCGCCACTGC CAGCGCCTTG ATGTGCTCTG CTGCTTCTCC AGGTACTGCC TGCGCCCCAG CCCCTTCCTC CCGTGACCCA CCATCCTGCC TCCCCAAGCC CACCTGGTGC CCCCACCTTC TGACCCACTG GGCTCTGAGC TCTTCAGCCC TGGAGGGTCC ACACGGGACC TTCTAGGCCA GGACTCGGAG GGGAAGTGAG GTGAAACTGT GCCGGGGAGG GAACACTGGA CTCCCGTCCA GGGGTGAGAC AGGACCGTCC TCGCGTACCC GCTCACAGAC ATGTCGGACC TGGATGCCGC CGCGGTGACG GTCGCGGAAC TACACGAGAC GACGAAGAGG TCCATGACGG ACGCGGGGTC GGGGAAGGAG GGCACTGGGT 1501 CCTGAGCCTC CCCTTCACTC CACTTTGACA CGGCCCCTCC CTTGTGACCT GAGGCAGGT CCCCACTCTG TCCTGGCAGG AGCGCATGGG CGAGTGTCTG CTAGGACGGG CAGGAGCTGG GGGACGGGAC AGTACCAGTG GGCATTGCCC ACCTCACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGGTCA GTACACCAGT GGTAGGACGG AGGGGTTCGG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAAGTCGGG ACCTCCCAGG TGTGCCCTGG AAGATCCGGT 2101 GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCTG CCCTGTGCCC GCTGGAATCT TGCCCATTTC GCCGGCTATC AGTTTGCCCC GTTGCTGCTC CAACGACGAG 2201 CAGTCACATG CCAAGGCCAT CGTGCTGGTG CTCTTTGGTG CTCTTCTGGG CCTGAGCCTC TACGGAGCCA CCTTGGTGCA AGACGGCCTG GCCCTGACGG GTCAGTGTAC GGTTCCGGTA GCACGACCAC GAGAACCAC GAGAAGACCC GGACTCGGAG ATGCCTCGGT GGAACCACGT TCTGCCGGAC CGGGACTGCC STCCTCGACC CCCTGCCCTG TCATGGTCAC CCGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAAATGGG TGACACTTCG GTCGTCGGTC CGGGCGATAG TCAAACGGGG CCTCCTCCTC TGTTCCGTCT TCCGTCGGAC GTTCAGGGAC GGGACACGGG CGACCTTAGA ACGGGTAAAG 1901 2001 1801

# FIG.\_ 10C

2301 ATGTGGTGCC TCGGGGCACC AAGGAGCATG CCTTCCTGAG CGCCCAGCTC AGGTACTTCT CCCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA TACACCACGG AGCCCCGTGG TTCCTCGTAC GGAAGGACTC GCGGGTCGAG TCCATGAAGA GGGACATGCT CCACCGGGAC CACTGGGTCC CACCGAAACT

2401 CTACGCCCAC TCCCAACGCG CCCTCTTTGA TCTGCACCAG CGCTTCAGTT CCCTCAAGGC GGTGCTGCCC CCACCGGCCA CCCAGGCACC CCGCACCTGG GATGCGGGTG AGGGTTGCGC GGGAGAAACT AGACGTGGTC GCGAAGTCAA GGGAGTTCCG CCACGACGGG GGTGGCCGGT GGGTCCGTGG GGCGTGGACC

2501 CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA GGACTGGGCT TCTGGGCGCA TCACCCGCCA CTCGTACCGC AATGGCTCTG

GACGTGATAA TGGCGTTGAC CGATGTCCCT TAGGTCCGAC GGAAACTGGT CCTGACCCGA AGACCCGCGT AGTGGGCGGT GAGCATGGCG TTACCGAGAC

AGGATGGGGC CCTGGCCTAC AAGCTGCTCA TCCAGACTGG AGACGCCCCTGG ATTTCAGCCA GGTTGGGAGA GGGCTGGAGG GGTCCACTAG GGACCGGATG ITCGACGAGT AGGICTGACC ICTGGGGTC CTCGGAGACC TAAAGTCGGT CCAACCCICT CCCGACCTCC CCAGGTGATC 2601

2701 TACAGGGGCT GCAGGCCTCC TGGGCCCAGG CCTTCAGCCC TCTCTGCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGGACT GATTCCACCC CGTCCGGAGG ACCCGGGTCC GGAAGTCGGG AGAGACGGAG ACGTCGACTG GTGTTCCTTC GACCACCTGT CTCTCCTGA CTAAGGTGGG

2801 GAGCTCTTCT ACATGGGGCT GACCGTGTGG GTGAGCAGTG ACCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCCT GAAGGCTGC CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGGACCC AGACCGTCGG AGTGTCCGGT TGAAGATGGG GGGTGGAGGA CTTACCGACG

2901 ACGACAAATA CGACACCACG GGGGAGAACC TTCGCAGTGA GTCTTGGGGG GAGCTCGGCA AGAGCCTCAG CCTCGCCCCAC ACAAGCCCTG AGCCTGAGGC TGCTGITIAI GCTGTGGTGC CCCCTCTTGG AAGCGTCACT CAGAACCCCC CTCGAGCCGT TCTCGGAGTC GGAGCGGGTG TGTTCGGGAC

3001 CCTGCCCACT CTGCCCCGTG CTCACGGCCC TGTCCCTCTCTCC CTTCCCCTCC CCTCCACAGT CCGGCCAGCT CAGCCCTTGG AGTTTGCCCA GGACGGGTGA GACGGGGAC GAGTGGCGGG ACAGGGAGAG GGAGAAGAGG GAAGGGGGAGG GGAGGTGTCA GGGCGGTCGA GTCGGGAACC TCAAACGGGT

3101 GTYCCCCTYC CIGCYGCGYG GCCYCCAGAA GACYGCAGAC TYYGYGGAGG CCAYCGAGGG GGCCCGGGCA GCAYGCGCAG AGGCCGGCCA GGCYGGGGYG CAAGGGGAAG GACGACGCAC CGGAGGTCTT CTGACGTCTG AAACACCTCC GGTAGCTCCC CCGGGCCGT CGTACGCGTC TCCGGCCGGT CCAACCCCAC

GTGCGGATGG GGTCGCCGAG GGGGAAGGAG AAGACCCTTG TCATAGACCC GGACGCCGCG ACGAAGGACG ACCGGCAGAC GTAGGACGAC CACACGTGAA CACGCCTACC CCAGCGGCTC CCCCTTCCTC TTCTGGGAAC AGTATCTGGG CCTGCGGGGG TGCTTCCTGC TGGCCGTCTG CATCCTGCTG GTGTGCACTT 3201

TOCTOGICTG TGCTCTGCTG CTCCTCAACC CCTGGACGGC TGGCCTCATA GTGAGTGCTT GCAGGAGTGG GGACAGAGAC ACCCCACCCT TCCCTGCCCA 3301

AGGAGCAGAC ACGAGACGAC GAGGAGTTGG GGACCTGCCG ACCGGAGTAT CACTCACGAA CGTCCTCACC CCTGTCTCTG TGGGGTGGGA AGGGACGGGT

CGGACAGTAG GGAGGACGGT CCTCGGGAGA CACTCGGGAC AGAGGGAGTC CACGACCAGG ACCGCTACTA CTGTCACCTT GAGAAACCAT AGTACCCAAA 3401 GCCTGTCATC CCTCCTGCCA GGAGCCCTCT GTGAGCCCTG TCTCCCTCAG GTGCTGGTCC TGGCGATGAT GACAGTGGAA CTCTTTGGTA TCATGGGTFT

CCIGGGCATC AAGCIGAGIG CCATCCCCGI GGIGATCCIT GIGGCCICIG TAGGCAITGG CGITGAGITC ACAGICCACG IGGCICTGGI GAGCACGGGC GGACCCGTAG TICGACICAC GGIAGGGGCA CCACTAGGAA CACCGGAGAC AICCGIAACC GCAACICAAG IGICAGGIGC ACCGAGACCA CICGIGCCCG 3501

3601 ACCCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTTC AAGCCCCTAC TATGTGCTAG GTACTATTTA AGAATTTGGG CTGGGTGGAC CCCTGGTTAG TCGACTAAGT CATAAGTTGT GTATAACAAG TTCGGGGATG ATACACGATC CATGATAAAT TCTTAAACCC GACCCACCTG

GIGGIGGCIC AITCCIGIAA ICCCAGCACT IIGGGAGGCC GAGGCGGGIG GAICACCIGA GGICGGGAGI ICGAAACCAG CCIGGCCAAC AIGGIGAAAC CACCACCGAG TAAGGACATT AGGGTCGTGA AACCCTCCGG CTCCGCCCAC CTAGTGGACT CCAGCCCTCA AGCTTGGTC GGACCGGTTG TACCACTTTG 3701

CCTGTCTTTA CTAAAAATAC AAAAATTAG CCAGGCGTGG TGGCACATGC CAGTAGTCCC AGCTACTTTG GAGGCTGAGG CAGAATTGCT GATITITIATG TITITIAATC GGICCGCACC ACCGIGIACG GICAICAGGG ICGAIGAAAC CICCGACTCC GICITAACGA 3801

3901

TCCGCTTCCA ACGTCACTCG ACTCTAGCAC GGTAACGTGA GGTCGGACCC GTTGTTCTCA CGTTGAGAGG CAGAGTTTTT TTTTTTTTT TTCCCGCCGG GCGA 4001

CCCC

1 TTCCGGCATG ACTCGATCGC CGCCCTCAG AGAGCTGCCC CCGAGTTACA CACCCCCAGC TCGAACCGCA GCACCCCAGA TCCTAGCTGG GAGCCTGAAG AAGGCCGTAC TGAGCTAGCG GCGGGGAGTC TCTCGACGGG GGCTCAATGT GTGGGGGTCG AGCTTGGCGT CGTGGGGTCT AGGATCGACC CTCGGACTTC 101 GCTCCACTCT GGCTTCGTGC TTACTTCCAG GGCCTGCTCT TCTCTCTGGG ATGCGGGATC CAGAGACATT GTGGCAAAGT GCTCTTTCTG GGACTGTTGG cgaggtgaga ccgaagcacg aatgaaggtc ccggacgaga agagagccc tacgccctag gtctctgtaa caccgtttca cgagaaagac cctgacaacc

201 CCTTTGGGGC CCTGGCATTA GGTCTCCGCA TGGCCATTAT TGAGACAAC TTGGAACAGC TCTGGGTAGA AGTGGGCAGC CGGGTGAGCC AGGAGCTGCA GGAAACCCCG GGACCGTAAT CCAGAGGCGT ACCGGTAATA ACTCTGTTTG AACCTTGTCG AGACCCATCT TCACCCGTCG GCCCACTCGG TCCTCGACGT

301 TTACACCAAG GAGAAGCTGG GGGAGGAGGC TGCATACACC TCTCAGATGC TGATACAGAC CGCACGCCAG GAGGGAGAGA ACATCCTCAC ACCCGAAGCA TGTAGGAGTG TGGGCTTCGT AATGIGGITC CICITCGACC CCCTCCTCCG ACGIATGIGG AGAGICTACG ACTAIGICTG GCGIGCGGIC CICCCICTCT

CTIGGCCTCC ACCTCCAGGC AGCCCTCACT GCCAGTAAAG TCCAAGTATC ACTCTATGGG AAGTCCTGGG ATTTGAACAA AATCTGCTAC AAGTCAGGAG TTCAGTCCTC TGGAGGTCCG TCGGGAGTGA CGGTCATTTC AGGTTCATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG 401

TICCCCTIAT TGAAATGGA ATGATTGAGT GGATGATTGA GAAGCTGTTT CCGTGCGTGA TCCTCACCCC CCTCGACTGC TTCTGGGAGG GAGCCAAACT AAGGGGAATA ACTTITACCT TACTAACTCA CCTACTAACT CTTCGACAAA GGCAGGCACT AGGAGTGGGG GGAGCTGACG AAGACCCTCC CTCGGTTTGA 501

FIG.\_11A

GGTTCCCCCG AGGCGGATGG ACGGGCCGGC GGGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGGAGGAA 601 CCAAGGGGG TCCGCCTACC TGCCCGGCCG CCCGGATATC CAGTGGACCA ACCTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCTT

CTCCCGAAGG CCCTCGACGA TCTGTTCCGT GTCCACCCGG TCCGGATGCA CCCCGCCGGG ACAGACGTGG GACTACTGGA GGTGACGGGT GGATCACGGG 701 GAGGGCTTCC GGGAGCTGCT AGACAAGGCA CAGGTGGGCC AGGCCTACGT GGGGGGGCCC TGTCTGCACC CTGATGACCT CCACTGCCCA CCTAGTGCCC

CCAACCATCA CAGCAGGCAG GETCCCAATG TGGCTCACGA GCTGAGTGGG GGCTGCCATG GCTTCTCCCA CAAATTCATG CACTGGCAGG AGGAATTGCT GGTTGGTAGT GTCGTCCGTC CGAGGGTTAC ACCGAGTGCT CGACTCACCC CCGACGGTAC CGAAGAGGGT GTTTAAGTAC GTGACCGTCC TCCTTAACGA 801

CGACCCTCCG TACCGGTCTC TGGGGGTTCC TCTCGACGAC TCCCGTCTCC GGGACGTCTC GTGGAAGAAC GACTACTCAG GGGCGGTCGA CATGCTCGTA GCTGGGAGGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGGCAGAGG CCCTGCAGAG CACCTTCTTG CTGATGAGTC CCCGCCAGCT GTACGAGCAT 901

1001 TTCCGGGGTG ACTATCAGAC ACATGACATT GGCTGGAGTG AGGAGCAGGC CAGCACAGTG CTACAAGCCT GGCAGCGGCG CTTTGTGCAG CTGGCCCAGG AAGGCCCCAC TGATAGTCTG TGTACTGTAA CCGACCTCAC TCCTCGTCCG GTCGTGTCAC GATGTTCGGA CCGTCGCCGC GAAACACGTC

PCCGGGACGG ACTCTTGCGA AGGGTCGTCT AGGTACGGAA GAGGAGGTGG TGGACCTAT TGTAGGACGT ACGCAAGAGA CTTCAGTCAC GACGGGCACA 1101 AGGCCCTGCC TGAGAACGCT TCCCAGCAGA TCCATGCCTT CTCCTCCACC ACCCTGGATA ACATCCTGCA TGCGTTCTCT GAAGTCAGTG CTGCCCGTGT

CCACCTICCG ATAGACGAGT ACGACCGGAT ACGGACACAC TGGTACGACG CCACCCTGAC GCGGGTCAGG GTCCCAAGGC ACCCGGAACG GCCCCATGAC 1201 GGTGGGAGGC TATCTGCTCA TGCTGGCCTA TGCCTGTGTG ACCATGCTGC GGTGGACTG CGCCCAGTCC CAGGGTTCCG TGGGCCTTGC CGGGGTACTG

CTGGTGGCCC TGGCGGTGGC CTCAGGCCTT GGGCTCTGTG CCCTGCTCGG CATCACCTTC AATGCTGCCA CTACCCAGGT GCTGCCCTTC TTGGCTCTGG GACCACCGGG ACCGCCACCG GAGTCCGGAA CCCGAGACAC GGGACGAGCC GTAGTGGAAG TTACGACGGT GATGGGTCCA CGACGGGAAG AACCGAGACC 1301

FIG.\_ 11B

1401 GAATCGGCGT GGATGACGTA TTCCTGCTGG CGCATGCCTT CACAGAGGCT CTGCCTGGCA CCCCTCTCCA GGAGCGCATG GGCGAGTGTC TGCAGCGCAC CITAGCCGCA CCTACTGCAT AAGGACGACC GCGTACGGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGCGTAC CCGCTCACAG ACGTCGCGTG 1501 GGGCACCAGT GTCGTACTCA CATCCATCAA CAACATGGCC GCCTTCCTCA TGGCTGCCCT CGTTCCCATC CCTGCGCTGC GAGCCTTCTC CTTACAGCCA CCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCGG CGGAAGGAGT ACCGACGGGA GCAAGGGTAG GGACGCGACG CTCGGAAGAG GAATGTCGGT 1601 TCCTCAGCCT GGACCTACGG CGGCGCCACT GCAGCGCCT TGATGTGCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCA AGGAGTCGGA CCTGGATGCC GCCGCGGTGA CGGTCGCGGA ACTACACGAG ACGACGAAGA GGTCAGGGAC GAGACGAGTC CACTAAGTCT AGGACGGGGT

GGAGCTGGGG GACGGGACAG TACCAGTGGG CATTGCCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGGTCACC CCTCGACCCC CTGCCCTGTC ATGGTCACCC GTAACGGGTG GAGTGACGGT GTCAAGTTCG GAAATGGGTG ACACTTCGGT CGTCGGTCGT ACACCAGTGG 1701

1801 ATCCTGCCTC CCCAAGCCCA CCTGGTGCCC CCACCTTCTG ACCCACTGGG CTCTGAGCTC TTCAGCCCTG GAGGGTCCAC ACGGGACCTT CTAGGCCAGG TAGGACGGAG GGGTTCGGGT GGACCACGGG GGTGGAAGAC TGGGTGACCC GAGACTCGAG AAGTCGGGAC CTCCCAGGTG TGCCCTGGAA GATCCGGTCC

1901 AGGAGGAGAC AAGGCAGAAG GCAGCCTGCA AGTCCCTGCC CTGTGCCCGC TGGAATCTTG CCCATTTCGC CCCGGAATTC CTGCAGCCCG GGGATCCAC TICCGICITC CGICGGACGI ICAGGGACGG GACACGGGCG ACCITAGAAC GGGTAAAGCG GGGCCTIAAG GACGICGGGC CCCTAGGIG rccrccrcrg

ATCAAGATCT CGCCGGCGGT GGCGCCACCT CGAGGTCGAA AACAAGGGAA ATCACTCCCA ATTAACGCGC GAACCCATAG AA 2001 TAGITCTAGA GCGGCCGCCA CCGCGGTGGA GCTCCAGCTT TTGTTCCCTT TAGTGAGGGT TAATTGCGCG CTTGGGTATC

FIG.\_ 11C

>

TGCAGTGAAA

TGTTGATCTT ACGTCACTTT

1 GITAITICAG GCCATGGIGI IGCGCCGAAT TAAITCCCGA TCCAGACAIG ATAAGAIACA ITGATGAGIT IGGACAAACC ACAACTAGAA

CGGTACCACA ACGCGGCTTA ATTAAGGGCT AGGTCTGTAC TATTCTATGT AACTACTCAA ACCTGTTTGG

CAATAAAGTC

101

TITIACGAAA TAAACACTIT AAACACTACG ATAACGAAAT AAACATIGGT AATATICGAC GITATITGIT CAACCCGGIA CCGCCGGITC GAAGACGICC

AAAATGCTTT ATTTGTGAAA TTTGTGATGC TATTGCTTTA TTTGTAACCA TTATAAGCTG CAATAAACAA

201 TCGACTCTAG AGGATCCCCG GGGAATTCCG GCATGACTCG ATCGCCGCCC CTCAGAGAGC TGCCCCCGAG TTACACACCC AGCTGAGATC TCCTAGGGGC CCCTTAAGGC CGTACTGAGC TAGCGGGGGG GAGTCTCTCG ACGGGGGCTC AATGTGTGGG

CCAGCTCGAA CCGCAGCACC

GGCGTCGTGG

GGTCGAGCTT

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CTTCTGCAGG

GTTGGGCCAT GGCGGCCAAG

TGTAACACCG GTAGAAGTGG CATCTTCACC O I GGGGCCCTGG CATTAGGTCT CCGCATGGCC ATTATTGAGA CAAACTTGGA ACAGCTCTGG TGTCGAGACC CCTAGGTCTC O J α TAATAACTCT GTTTGAACCT GACCCTACGC U ပ Z CGAGAAGAGA ഗ ы ĹĽ L) GCACGAATGA AGGTCCCGGA GTAATCCAGA GGCGTACCGG K Σ 0 ĸ × O K K ᆸ TGAGACCGAA CCCGGGGACC æ ပ 401 AAAGTGCTCT TTCTGGGACT GTTGGCCTTT TTTCACGAGA AAGACCCTGA CAACCGGAAA CGACCCTCGG ACTTCCGAGG ĹĻ Ø × **.**.. ນ ເວ ഗ GGTCTAGGAT > O 57 24

301 CCAGATCCTA GCTGGGAGCC TGAAGGCTCC ACTCTGGCTT CGTGCTTACT TCCAGGGCCT GCTCTTCTCT CTGGGATGCG GGATCCAGAG ACATTGTGGC

CAGACCGCAC GCCAGGAGGG GTCTGGCGTG CGGTCCTCCC Ģ ш Ø æ CTACGACTAT GAGCCAGGAG CTGCATTACA CCAAGGAGAA GCTGGGGGAG GAGGCTGCAT ACACCTCTCA GATGCTGATA ,, Σ CTCCGACGTA TGTGGAGAGT 0 ഗ Ø æ ы AGTICCICIT CGACCCCCIC ပ .. (r.) × GACGTAATGT I CTCGGTCCTC Ø ഗ 501 GCAGCCGGGT CGTCGGCCCA S 3

CCTCCACCTC CAGGCAGCCC TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC CTGGGATTTG GACCCTAAAC :≥ GGAGGTGGAG GTCCGTCGGG AGTGACGGTC ATTTCAGGTT CATAGTGAGA TACCCTTCAG × ტ ᆸ ഗ O > × Ø Ę Ø A 0 ٦, . H CTCACACCCG AAGCACTTGG TTCGTGAACC ပ ... TCTCTTGTAG GAGTGTGGGC a, €~ 601 AGAGAACATC z ោ 124

ACCCCCCTCG TGGGGGGAGC u CITATIGAAA AIGGAAIGAI IGAGIGGAIG AIIGAGAAGC IGIIIICCGIG CGIGAICCIC GCACTAGGAG н > TAACTCTTCG ACAAAGGCAC O ľ × <u></u>ы Н GAATAACTIT TACCTTACTA ACTCACCTAC Σ 3 ĹĴ × ပ ជ Н 701 AACAAATCT GCTACAAGTC AGGAGTTCCC TCCTCAAGGG Δ, **:**> O CGATGTTCAG × TTGTTTAGA 157

AAACTCCAAG GGGGCTCCGC CTACCTGCCC GGCCGCCCGG ATATCCAGTG GACCAACCTG GATCCAGAGC AGCTGCTGGA CTAGGTCTCG TCGACGACCT 4 CTGGTTGGAC z CCTCCCTCGG TITGAGGITC CCCCGAGGCG GATGGACGGG CCGGCGGGCC TATAGGICAC ပ æ ഗ ပ 1. Q 801 ACTGCTTCTG GGAGGGAGCC O TGACGAAGAC U 191

5 2005

TACGTGGGG GGCCCTGTCT GCACCCTGAT CGTGGGACTA I CCGGGACAGA O GGGAAACGGA GGGAACTCCC GAAGGCCCTC GACGATCTGT TCCGTGTCCA CCCGGTCCGG ATGCACCCCG ပ > \* GGAGCTGGGT CCCTTTGCCT CCCTTGAGGG CTTCCGGGAG CTGCTAGACA AGGCACAGGT GGGCCAGGCC Ø ഠ > O Ω ρź ſμ ជេ 901 224

TCCCACAAAT AGGGTGTTTA × ä GGTACCGAAG GIGGGGCTG CCATGGCTTC ഠ CACCCCCGAC ഗ ഗ CACGAGCTGA GTGCTCGACT ш GACCTCCACT GCCCACCTAG TGCCCCCAAC CATCACAGCA GGCAGGCTCC CAATGTGGCT CTGGAGGTGA CGGGTGGATC ACGGGGGTTG GTAGTGTCGT CCGTCCGAGG GTTACACCGA K > 2 4 0 ഗ H Z Q, U 1001 257

AGAGGCCCTG CAGAGCACCT TCTTGCTGAT GTCTCGTGGA AGAACGACTA ü ... TCTCCGGGAC LI A ធ CGTCCTCCTT AACGACGACC CTCCGTACCG GTCTTGGGG GTTCCTCTGG ACGACTCCCG THECHGE GAGGEATGGE CAGAGACCCE CAAGGAGAG TGETGAGGGC K œ ပ C C B B B .i .i 1101 TCATGCACTG GCAGGAGGAA [1] AGTACGTGAC 291 CAGGCCAGCA CAGTGCTACA AGCCTGGCAG GTCCGGTCGT GTCACGATGT TCGGACCGTC 3 ت > e ഗ « « GAGTGAGGAG CTCACTCCTC ы EŲ. ഗ CCCACTGATA GTCTGTGTAC TGTAACCGAC CAGCTGTACG AGCATTTCCG GGGTGACTAT CAGACACATG ACATTGGCTG 3 တ н X E O χ Ω ഗ CTCAGGGGG GTCGACATGC TCGTAAAGGC ᄄ (1) ν C C GAGTCCCCGC 1201 324

CTGCATGCGT GACGTACGCA L H A CGGCGCTTTG TGCAGCTGGC CCAGGAGGCC CTGCCTGAGA ACGCTTCCCA GCAGATCCAT GCCTTCTCCT CCACCACCCT GGATGACATC CCTACTGTAG Ω GCCGCGAAAC ACGTCGACCG GGTCCTCCGG GACGGACTCT TGCGAAGGGT CGTCTAGGTA CGGAAGAGGA GGTGGGAA H ۲ £τ, I н or Or M ם Ø ы α 0 (L 1301 357

TOTOTERAMET CAGTECC CETETGETEG GAGGOTATOT GOTCATGOTG GOOTATGOOT GIGTGACCAT GOTGCGGTGG GACTGCGCCC AGTCCCAGGG TCAGGGTCCC CTGACGCGGG υ Ω GTCACGACGG GCACACCACC CTCCGATAGA CGAGTACGAC CGGATACGGA CACACTGGTA CGACGCCACC 3 α, Ļ Σ E > A Y A ľ M ჯ უ R V V A A ഗ AGAGACTTCA 1401 

ACGGTGATGG TGCCACTACC AAGGCACCCG GAACGGCCCC ATGACGACCA CCGGGACCGC CACCGGAGTC CGGAACCCGA GACACGGGAC GAGCCGTAGT GGAAGTTACG CTTGCCGGGG TACTGCTGGT GGCCCTGGCG GTGCCTCAG GCCTTGGGCT CTGTGCCCTG CTCGGCATCA CCTTCAATGC K Z ပ æ U 0 0 ۲., S A > 'A L A r. > ᆸ ა ა TTCCGTGGGC ပ 1501 424

GAGGTCCTCG CTCCAGGAGC Ø GTCCACGACG GAAGAACCG AGACCCTTAG CCGCACCTAC TGCATAAGGA CGACCGCGTA CGGAAGTGTC TCCGAGACGG ACCGTGGGGA TGGCACCCCT CAGGIGCTGC CITTCTTGGC TCTGGGAATC GGCGTGGATG ACGTATTCCT GCTGGCGCAT GCCTTCACAG AGGCTCTGCC ... K (L Æ L A > Ω > 0 ഗ ↵ r, A **(1**4 > 1601 457

CCTCATGGCT GCCCTCGTTC CCATCCCTGC GCGTGCCCGT GGTCACAGCA TGAGTGTAGG TAGTTGTTGT ACCGGCGGAA GGAGTACCGA CGGGAGCAAG GGTAGGGACG ۵, Σ آجر GTGTCTGCAG CGCACGGGCA CCAGTGTCGT ACTCACATCC ATCAACAACA TGGCCGCCTT Σ Z z ₽ L > : CGTACCCGCT CACAGACGTC 1701 GCATGGGCGA 497

FIG. 1B

GCTGGTGGAC AGAGAGGGAC TGATTCCACC CGAGCTCTTC GCTCGAGAAG CGACCACCTG TCTCTCCCTG ACTAAGGTGG Ø 田田 ; ; TCTGGATTTC AGCCAGCTGA CCACAAGGAA AGACCTAAAG TCGGTCGACT GGTGTTCCTT ب. o s Ω TGACCTCTGC GGGTCCTCGG CCCAGGAGCC 2701 GCTCATCCAG ACTGGAGACG CGAGTAGGTC 824 GETGAGCAGT GACCCCTGG GTCTGGCAGC CTCACAGGCC AACTTCTACC CCCCACCTCC TGAATGGCTG CACGACAAAT GTGCTGTTTA TTGAAGATGG GGGGTGGAGG ACTTACCGAC പ a, <u>بر</u> CCACTCGTCA, CTGGGGGACC CAGACCGTCG GAGTGTCCGG **A** ഗ Ω ഗ ഗ > TGACCGTGTG ACTGGCACAC > ATGTACCCCG TACATGGGGC 2801 857

CTCCAGAAGA CTGCAGACTT GACGTCTGAA Д GAGGTCTTCT CTTCGCATCC CGCCAGCTCA GCCCTTGGAG TTTGCCCAGT TCCCCTTCCT GCTGCGTGGC CGGGAACCTC AAACGGGTCA AGGGGAAGGA CGACGCACCG ပ α rı Lı മ 0 ω ے D. GAAGCGTAGG GCGGTCGAGT æ CCCCCTCTTG GGGGGAGAAC z [1] ACGACACCAC TGCTGTGGTG (a 2901 891

CTGGGAACAG 0 ANGOGCAGAG GCCGGCCAGG CTGGGGTGCA CGCCTACCCC AGCGGCTCCC CCTTCCTT TCGCCGAGGG GGAAGGAGAA ᇤ Œ O TACGCGTCTC CGGCCGGTCC GACCCCACGT GCGGATGGGG × ï တ O ഗ O CCCGGGCAGC TAGCTCCCCC GGGCCCGTCG æ ATCGAGGGGG TGTGGAGGCC ACACCTCCGG ſЦ 3001 924

CACGTGAAAG GAGCAGACAC GAGACGACGA GGAGTTGGGG ACCTGCCGAC TGGACGGCTG ٤ CCTCAACCCC z ے GCCGTCTGCA TCCTGCTGGT GTGCACTTTC CTCGTCTGTG CTCTGCTGCT H U ۲ > Ľ ٤ O CGGCAGACGT AGGACGACCA > ATAGACCCGG ACGCCGCGAC GAAGGACGAC TGCGGCGCTG CTTCCTGCTG ᇦ L ĸ ĸ TATCTGGGCC 3101

GCGATGATGA CAGTGGAACT CTTTGGTATC ATGGGTTTCC TGGGCATCAA GCTGAGTGCC ATCCCCGTGG TGATCCTTGT ACTAGGAACA TAGGGGCACC CGACTCACGG ഗ CECTACTACT GTCACCTTGA GAAACCATAG TACCCAAAGG ACCCGTAGTT × ω Σ e E Ĺ ω > Σ Σ GCTGGTCCTG CGACCAGGAC GCCTCATAGT CGGAGTATCA 3201

CCAGGGCAGC CGGAACCTGC GGGCCGCCCA TGCCCTTGAG ACGGGAACTC GENCCCETICG GCCTTGGACG CCCGGCGGT z ပ α AGTCCACGTG GCTCTGGGCT TCCTGACCAC CGAGACCCGA AGGACTGGTG ᆸ ပ TCAGGTGCAC GGCATTGGCG TTGAGTTCAC CCGTAACCGC AACTCAAGTG Ĺ ပ CCGGAGACAT GGCCTCTGTA 3301

ATGAAGAAAC GTAACATTCC CATTGTAAGG > GCTGGTTCCC ACTTTGACTT TGAAACTGAA CGACCAAGGG ATCTCCACAT TGCTGGGTCT GCTCATGCTT TAGAGGTGTA ACGACCCAGA CGAGTACGAA Σ 0 L CGATGGGGCC GCTACCCCGG ် ပ Ω CACACATTTG CCCCCGTGAC GTGTGTAAAC GGGGGCACTG 3401

GGCGGTCTCC ACTATGTCTA TGATACAGAT CCGCCAGAGG CCTGGGCCCG TCACGAGTGC GAGGACCCGG AGGAGGTACC TGAGCACGAC GACGGACACG ACGACAGGTA GGACCCGGGC ഗ TGCTGTCCAT CTCCTGGGCC TCCTCCATGG ACTCGTGCTG CTGCCTGTGC G H G i v ᆸ 3501 CGGCGCTGAC AGTGCTCACG GCCGCGACTG 1091

FIG. 1D

3501 GTACAAGGAA AGCCCAGAGA TCCTGAGTCC ACCAGCTCCA CAGGGAGGCG GGCTTAGGTG GGGGGCATCO TCCTCCCTGC CCCAGAGCTT TGCCAGAGTG TGGTCGAGGT GTCCCTCCGC CCGAATCCAC CCCCGTAGG AGGAGGGACG GGGTCTCGAA ACGGTCTCAC O Ļ ပ ø d K <sub>ር</sub> TCGGGTCTCT AGGACTCAGG ഗ CATGTTCCTT 1124

CGGTGATCGA 3701 ACTACCTCCA TGACCGTGGC CATCCACCCA CCCCCCTGC CTGGTGCCTA CATCCATCCA GCCCCTGATG AGCCCCTTG GTCCCCTGCT GCCACTAGCT ۲ TGATGGAGGT ACTGGCACCG GTAGGTGGGT GGGGGGACG GACCACGGAT GTAGGTAGGT CGGGGACTAC TCGGGGGAAC CAGGGGACGA ഗ D. I > 1157

3801 CTGGCAACCT CAGTTCCAGG GGACCAGGTC CAGCCACTGG GTGAAAGAGC AGCTGAAGCA CAGAGACCAT GTGTGGGGCG TGTGGGGTCA CTGGGAAGCA

CONGENCOAG GICGGIGACC CACTITOTOG ICGACTICGI GICTOTGGIA CACACCOGG ACACCCCAGI GACCCTICGI ۲ æ Д GACCGTTGGA GTCAAGGTCC ഗ თ

1191

GACCCAGACC ACAATUTGUG TUUTGUCTGG GGAUCTUCCG GGAUGAUGAU GAUGTAGGGG AGAGGGUTGG GTUGACAGTA CUUGGAGGGA CTATAGCTTA CIGGGICTGG TGTTAGACGC AGGACGGACC CCTGCTGCTG CTGCATCCCC TCTCCCGACC CAGCTGTCAT GGGCCTCCCT GATATCGAAT 3901

4001 TCAATCGATA GAACCGAGGT GCAGTTGGAC AGTTAGCTAT CTTGGCTCCA CGTCAACCTG FIG. 1E

(SEQ ID NO: 3) 40. GCTGGGGTGCACGCCTACCNCAGCGGNTCCCCCTTCCTCTTCTGGGAACA \*\*\*\*\* ::: :: : CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA hpatched 3,040 GTATCTGGGCCTGCGGCGCTCTTCCTGCTGGCCGTCTGCATCCTGCTGG \* \*\*\*\* \*\* \* \*\*\* \* \*\*\* GTACATCGCCTCCGCCACTGGCTGCTGCTGTTCATCAGCGTGGTGTTGG hpatched 1.50 TGTGCACTTTCCTCGTCTGTGCTCTGCTGCTCCTNAACCCCTGGACGGCT CCTGCACATTCCTCGTGTGCGCTGTCTTCCTTCTGAACCCCTGGACGGCC hpatched GGCCTNATAGTGCTGGTCCTGGCGATGATGACAGTGGAACTCTTTGGTAT .905531 GGGATCATTGTGATGGTCCTGGCGCTGATGACGGTCGAGCTGTTCGGCAT hpatched CATGGGTTTNCTGGGCÁTCAAGCTGAGT \*\* \* \*\* \*\*\*\* GATGGGCCTCATCGGAATCAAGCTCAGT hpatched 

	80'	90	100	J	L10	120
905531	TCTGGGCCT	GCGGCGCT	GCTTCCTG	CTGGCCGT	CTGCATC	CTGCTGGTGT
	::: ::	*	** * **	****	. ****	* ** ***
hpatched	GCTGCTGCT	GTTCATCA	GCGTGGTG	TTGGCC-	TGCACAT	TCCTCGTGT
- L	309	0 3	100	3110	3 .	120
	130	140	150			
905531	GCACTTTCC	CTCGTCTGT	GCTCTGCT	GCT		
	** ** **	** *	: .	:		
hpatched	GCGCTGTCT	TCCTTCTG	AACCCCTG	GAC		
-	3130	3140	31.50			

GCTGGGGTGCACGCCTACCCCAGCGGCTCCCCTTCCTCTTCTGGGAACA ::: :: : CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTCATCAGCGTGGTGTTGG hpatched TGTGCACTTTCCTCNTCTGTGCTCT \*\*\*\* \*\*\*\*\* \*\* \*\* hpatched CCTGCACATTCCTCGTGTGCGCTGT 

> TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGTGT ::: ::: \* \*\* \* \*\* \*\*\* GCTGCTGCTGTTCATCAGCGTGGTGTTGGCC---TGCACATTCCTCGTGT hpatched GCACTTTCCTCNTCTGTGCTCT \*\* \*\* \*\* GCGCTGTCTTCCTTCTGAACCC hpatched

р П С TGGLRRAAAPDR....MTRSPPLR R T G (  $\alpha$  $\alpha$ Œ AGGG O.  $\alpha$ ഗ CIGAP 0000 ODRGGG ۵. w ⋖ AGNA MAS I (SEQ ID NO.2) PTCH2

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w w EVGGRVSRELNYTROKIGE EVGSRVSOELHYTKEKLGE V.V.GELETEGAFAVGEKAANLETNVEELWV FEGELEAFGAEAEGERMATTETNLEOLWV ц > Ц > 28 101 PTCH2 TIPEALGUHLOSALOASRVHVYMYNROWKL IPEALGUHLOAALTASKVOVSLYGKSMOL AMFNPOLMIOTPKEEGANV AAYTSQMUIOTARQEGENI 151 108 PTCH2

(O O H L C Y K S G E L I TETGY M D O I I EYLLYPOL II I T P L D C F W E G A K L O S G T A Y L L K I C Y K S G V P L I E N G M I E W M I E K L F P C V I L T P L D C F W E G A K L O G G S A Y L P 201 158 PTCH2 PTCH

LEELGPFA - SLEGFRELLDKAOVGAAYVGRPCLNPA KPPLRWTNFDPLEF RPDIOWINLOPEOL 251 208 PTCH2

ഗെല LNGGCHGLSRKYMHWQEELIVGGTVKN: LSGGCHGFSHKFMHWQEELLLGGMARDI D P D C P A T A P N K N S T K P L D M A L V O L H C P P S A P N H H S R Q A P N V A H E 301 257 PTCH2

TIGKILVSAHALOTMFOLMTPKOMYEHFKGYEYVSH.TINWNEDKAAAILEAW OGELLRAEALOSTFILLMSPROLYEHFRG.DYOTHOLIGMSEEQASTVLOAW 351 307 PTCH2

ORTYVEVVHOSVAQNSTOKVLSFTTTTLDDILKSFSDV3V | RVAS BAYLLM Orrfvolacealpenas oo 1 hafssittddilhafslevskaarv garlem 400 356 PTCH2 PTCH

Z တ ⊢ A L S V A A G L G L A L A V A S G L G L LAYACLTMLRWDGSKSOGAVGLAGVLLVAL LAYACVÍMERWDCAOSOGSVGLAGVLLVAL 406 PTCH2 PTCH

FLALGNOVDVELLAHAFSETGONKRIPFEDRTGECLKRTGAS FLALGNOVDDVELLAHAFTEALPG..TPLQERMGECLORTGTS 0 V L P F 1 0 V L 200 456 PTCH2 PTCH

A MIVILLE FRATESM VAIVMENERATEST SLOAAVVVV KRNE SLOAAHVVGCTE PIPALRAFS PIPALRAFS FAFEMAALIVIP LTS ISNVTA 504 989 PTCH

တလ 8 H S S > d >-a. o\_ ۵. o. S >-Œ LYRREDRRLD 1 FCCFTSPCVSRVIOVEPOAYTOTHDNT1 LRRBHCORLDVLCCFSSPCSAOVIO 1 LPOELGDGT - - -009 PTCH2 PTCH2 PTCH

ပေဖ ETQITMQSTVQLRTEYDPHTHVYYTTAEPRSEISVQPVTVTQDTLS A H H A u. 593 PTCH2

a. 0 DLLISOFSDSSLH - OLEPPOTKMTLSSFAEKHYAPFLLK DLLIGOEEETROKAACKSLPCARMNLAHFARYOFAPLLLO 0 S P E S T S S T R E L F S P G G S T R I 700 PTCH2 PTCH

S. Y.GTTRVRDGLDLTDIVPRETREYDFIAAGFKY SLYGATLVODGLALTDVVPRGTKEHAELSAGLRY KAKVVVII F HAKAIV 684 PTCH2 PTCH

K M W L H OLPK MWLO APRTWL MLEENKO FSFYNMY IVTOKA - DYPNIOHLLYDLHRSFSNVKYVMLEENK FSLYEVALVTOGGFDYAHSORALFDLHORFSSLKAVLPPPAT 798 PTCH2 PTCH

3B

a a 고 교 0 8 B D K 0 O > \_1 ¥ × ¥ ---YFROWLOGLODAFDSDWETGKIMPNNYKNGSDDGVIYYRNGSDDGVIYYRNGSEDGAL PTCH2 PTCH

م م <u>ac</u> a\_ I O OLTKORLVDADGIIINPSAFYIYLTAWVSNDPVAYAASQANIRPI OLTTRKLVDREGLIPPELFYMGLTVWVSSDPLGLAASQANFYPI 0 0 - 4 - 8 - 8 PTCH PTCH2

х 5 × С В В В PIEYAOFPFYLNGLADTSDFVEAIEP PLEFAOFPFLLRGLOKTAOFVEAIE \_ \_ \_ د 2 د ر ш Б П EWVHDKADYMPEWLHOKYD·TT 884 PTCH2 PTCH

HWLLLFISYVLACTFLVCA RCFLLAVOILLVCTFLVCA = WEQY | GLR ய ய F F 1 I CSNYTSLGLSSYPNGYP A CAEAGOAGVHAYPSGSP LLNPWTAGIIVMVLALMTVELFGMMGLIGIKLSAVPVVILTASVGIGVE LLNPWTAGLIVLVLAMMTVELFGIMMGFLGIKLSANPVVILVASVGIGVE PTCH2

GSEFIGSHFI LMLAC TM11 TVHVALAFLTA I GDKNARAVLALEHMFAPVLDGAVSTELGW TVHVALGFLTTOGSRNLRAAHALEHTFAPVTDGA I STLLGK 1097

٥. ப ப **∝** • zσ Y P E V S P A N G L N P P E V - O M Y K E S TM12 GVENGEVERPVEESFEGPY GFEHGEVEEPVEESFEGPP FAVIDATI FAVIDATVI ட்ட >-Œ Œ 1 > 1083 PTCH2

Ω  $\circ$ ⋖ o. ۵. G A Y H 0 S S D S E Y S S Q T T V S G L S A R V T T S M T V A I H P P P L P u, S G GHTHS SSLPOS ۵ ഗ WGAS FAMP SPEPPSVVRPPAPAPAPA 1197

FIG. 3C

PTCH 1247 AGG|PA|HQVIVEATENPVFAHSTVVHPESRHHPPSNPRQQPHLDSGSLPPG PTCH2 1182 PWS PAATSSGNLSSRGPGPATG

PTCH 1347 HNPRNPASTAMGSSVPGYCOPITTVTASASVÍVAVHPPPVPGPGRNPRGG 1297 ROGOOPRRDPPREGLWPPLYRPRRDAFEISTEGHSGPSNRARWGPRGARS PTCH 1397 L C P G Y P E I D H G L F E D P H V P F H V R C E R R D S K V E V I E L Q D V E C E E R P R G S S S PTCH 1447 N PTCH

FIG. 3E

Upper 👨

< 4.4 Kb

Lower

ط- β Actin

FIG. 4

1864

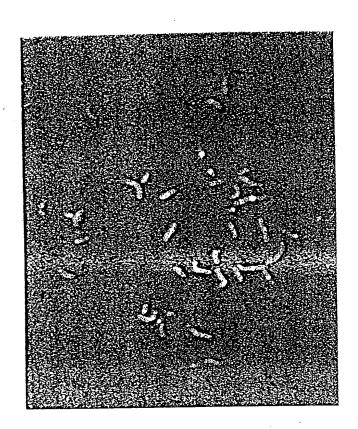
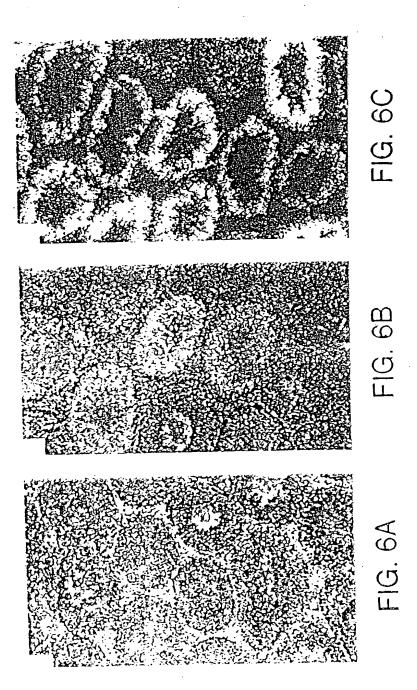
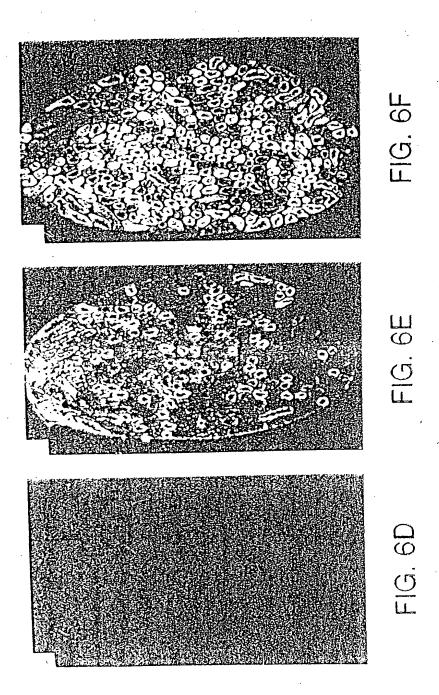
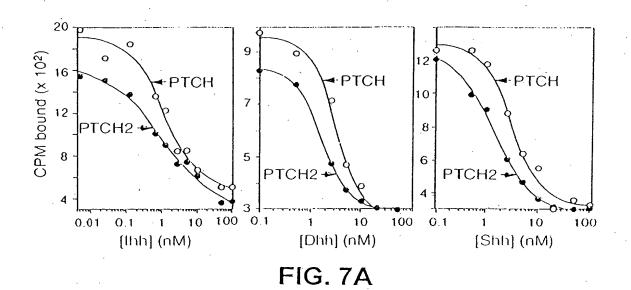


FIG. 5







IP Flag, Blot Myc

IP Flag, Blot Flag

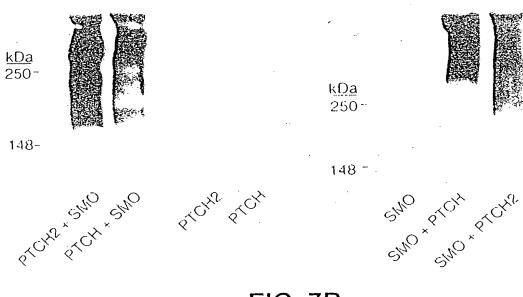


FIG. 7B

•		•			
	10	20	30	40	50
hPtch-2	MTRSPPLRELPPS	TPPARTAAPO	ILAGSLKAPI	WLRAYFQGLI	FSLGCG
	* * * ****				
mPatched2	MVRPLSLGELPPS				
(SEQ 1D NO:7)	10	20	3 0	4 0	50
	60	. 70	80	90	100
hPtch-2	IORHCGKVLFLGLI				
in ten 2	** *******	****	. * . * * * . * * *	****	****
mPatched2	IQKHCGKVLFLGLV	/AFGALALGLR	VAVIETDLEC	LWVEVGSRVS	
	60	70	80	90	100
	7.70	120	130	140	150
	110 KEKLGEEAAYTSQN	120 ALTOTAROEGE			
h <i>Ptch-</i> 2	**********	****	*.*****	****	****
mPatched2	KEKLGEEAAYTSQN				
	110	120	130	140	150
				3.00	200
	160 GKSWDLNKICYKS	170	180	190	CAKLOG 200
h <i>Ptcl1</i> -2	# * * * * * * * * * * * * * * * * * * *	* * * * * * * * * * * * * * * * * * *	* *******	*********	****
mPatched2	GKSWDLNKICYKS				
	160	170	180	190	200
			0.2.0	240	250
	210 GSAYLPGRPDIQW	220	230	240 PRELLOKAOVO	
h <i>Ptch</i> -2	**********	***** ***	*****	*****	***
mPatched2	GSAYLPGRPDIQW	TNLDPQQLLEI	ELGPFASLEGI	FRELLDKAQVO	QAYVGR
mr accricaz	210	220	230	240	250
	•				200
	260	270	280	290	300
h <i>Ptch</i> -2	PCLHPDDLHCPPS	APNHHSRQAPI *** *****	NVAHELISGGCI	* * * * * * * * * * * * * * * * * * *	/***** /5:::::::::::::::::::::::::::::::
mPatched2	PCLDPDDPHCPPS				
IllPatcheuz	260	270	280	290	300
•			.*		•
	310	320	330	340	. 350
hPtch-2	GMARDPQGELLRA	EALQSTFLLM	SPRQLYEHFR	GDYQTHDIGW:	SEEQAST
	* *** ** ***				
mPatched2	GTARDLQGQLLRA	EALQSTFLLM 320	330	340	350
	3·10	320	330		

FIG. 8A

		•				
	* 1 *	360	370	3.80	390	400
1	h <i>Ptch-</i> 2	VLQAWQRRFVQLA	QEALPENASQC	OIHAFSSTTLI	DDILHAFSEVS	SAARVVG
	•	****	****	****	**** ***	* . * * * *
Į	mPatched2	VLQAWQRRFVQLA	QEALPANASQQ 370	380	390	400
		360	3 7 0	300	370	400
		410	420	430	440	450
1	h <i>Ptch-</i> 2	GYLLMLAYACVTM	LRWDCAQSQGS	SVGLAGVLLV	ALAVASGLGL	CALLGIT
	•	****	*******	****	****	****
	mPatched2	GYLLMLAYACVTM	ILRWDCAQSQGA			
		410	420	430	440	450
		1.50	470	480	. 490	500
	t n. t.a	460 FNAATTQVLPFLA	470			
	h <i>Ptch</i> -2	*********	****	****	. * * * * * * * * *	**. ***
	mPatched2	FNAATTQVLPFLA				
		460	470	480	490	500
					5.10	550
-		510 SVVLTSINNMAAF	520	530	540	550 VEDATI
	h <i>Ptch</i> -2	SVVLTSINNMAAF	· ********	*****	**** * ***	****
	mPatched2	SVALTSVNNMVAF	FMAALVPIPAI	LRAFSLQAAI	VVGCNFAAVMI	LVFPAIL
	mr aconeac	510	520	530	540	550
		•				500
		560	570	580	590	000 VTATIUA
	hPtch-2	SLDLRRRHCQRLE	)VLCCFSSPC5/ +++++**	* * * * * * * * * * *	*** ***** FGDG1^E^G17	*****
	mDatabad?	SLDLRRRHRQRL	OVI.CCESSPCS	AOVIOMLPOE	LGDRAVPVGI	VTATJHA
	mPatched2	560	570	580	590	600
		610		630	640	650
	hPtch-2	QAFTHCEASSQH	VVTILPPQAHL'	VPPPSDPLGS	ELFSPGGSTR	DLLGQEE
		**************************************	****	*.***** r.c.n.c.n.c.	**.******	NILSOFF
	mPatched2		VVTTLPPQARL.		640	650
		610	020	030	0.10	
		660	670	680	690	700
	h <i>Ptch-</i> 2	"ETROKAACKSLP	CARWNLAHFAR	YQFAPLLLQS	HAKAIVLVLF	GALLGLS
.•		* .****	** * *****	***	*******	***
	mPatched2	GTGPQAACRPLL				GALLGLS 700
		660	670	680	690	700

	710	720	730	740	750
hPtch-2	LYGATLVQDGLAL	TDVVPRGTKE	HAFLSAQLRY	FSLYEVALVT	QGGFDYA
mPatched2	LYGATLVQDGLAL				
mpatched2	710	720	730	740	750
•					
_	760	770	780	790	008
h <i>Ptch-</i> 2	HSQRALFDLHQRF	SSLKAVLPPP *******	ATQAPKIWLH:	1 1 KNWLQG1Q1 *** ******	******
mPatched2	HSQRALFDLHQRF				
in accredz	760	770	780	790	800
	810	820	830	840	850
hPtch-2	ASGRITRHSYRNG	SEDGALAYKL	LIQTGDAQEPI	LDFSQLTTRKI	LVDREGL
	****				
mPatched2	ASGRITCHSYRNG 810	SEDGALAYKL 820	ETQTGNAQEP	840	850
	. 810	820	030	040	030
	860	870	088	890	, 900
h <i>Ptch</i> -2	IPPELFYMGLTVW	VSSDPLGLAA			
MFICH-Z	*****		·		
mPatched2	IPPELFYMGLTVW				
	860	870	880	890	900
	910	920	930	940	950
h <i>Ptch</i> -2	PAQPLEFAQFPFL	-			
III ICH Z	*****	* * * * * * * * *	*****	* . * * * * * * *	* * * * * *
mPatched2	AAQPLEFAQFPFL	LHGLQKTADF	VEAIEGARAA	CTEAGQAGVH	AYPSGSP
	910	920	930	940	950
		0.00	0.00	000	1000
1.0.1.0	960 FLFWEQYLGLRRC	970	980	990	1000 MMT 1111
h <i>Ptch</i> -2	FLFWEQYLGLRRC	.FLLAVCILLUV *********	****	* ******	*****
mPatched2	FLFWEQYLGLRRC				
mracchedz	960	970	980	990	1000
	, , ,				
	1010	1020	1030	1040	1050
h <i>Ptch-</i> 2	VELFGIMGFLGİK				
	*****				
mPatched2	VELFGIMGFLGI				HGSRNLR 1050
	1010	1020	. 1030	1040	1020

FIG. 8C

	1060	1070	1080	1090	1100		
h <i>Ptch-</i> 2	AAHALEHTFAPVTDGAISTLLGLLMLAGSHFDFIVRYFFAALTVLTLLGL						
<b></b>	** *** ****	***.****	*****	* * * * * * * * *	****		
mPatched2	AASALEQTFAPVT	DGAVSTLLGL	LMLAGSNFDF	IIRYFFVVLT	VLTLLGL		
	1060	1070	1080	1090	1100		
					,		
•	1110	1120	1130	1140	1150		
1 5. 1 5	LHGLVLLPVLLSI	LGPPPEVIQM	YKESPEILSP	PAPQGGGLRW	GASSSLP		
hPtch-2	****						
mPatched2	LHGLLLLPVLLSI	LGPPPQVVQV	YKESPQTLNS	AAPQRGGLRW	DRPPTLP		
	1110	1120	1130	1140	1150		
J	1160	1170		· ·	1200		
in to	OSFARVTTSMTVA	IHPPPLPGAY	IHPAPDEPPW	SPAATSSGNL	SSRGPGP		
h <i>Ptcl1-</i> 2	****				•		
mPatched2	OSFARVTTSMTVA	LHPPPLPGAY	VHPASEEPT	`			
. IIII accircae	1160	1170	1180	,			
	1100						
h <i>Ptch</i> -2	ATG						

FIG. 8D

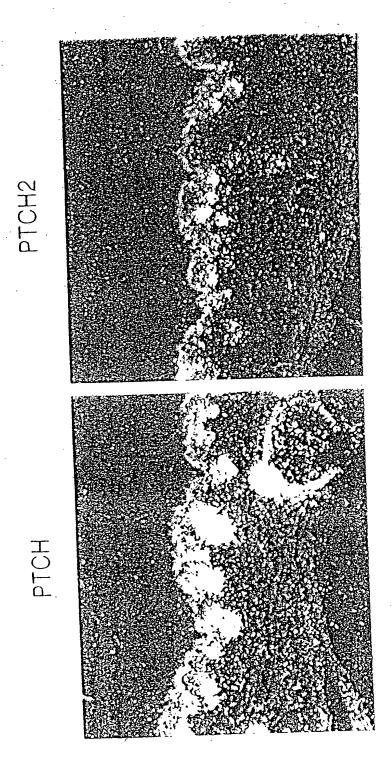


FIG. 9

d (BION OF DES)

1 CCCACGCGTC CGGGAGAAGC TGGGGGAGGA GGCTGCATAC ACCTCTCAGA TGCTGATACA GACCGCACGC CAGGAGGGAG AGAACATCCT CACACCGGAA ACGACTATGT CTGGCGTGCG GTCCTCCCTC TCTTGTAGGA GTGTGGGCTT GGGTGCGCAG GCCTCTTCG ACCCCCTCCT CCGACGTATG

101 GCACTIGGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAAGTCCT GGGAITTGAA CAAAATCTGC TACAAGTCAG CGTGAACCGG AGGTGGAGGT. CCGTCGGGAG TGACGGTCAT TTCAGGTTCA TAGTGAGATA CCCTTCAGGA CCCTAAACTT GTTTTAGACG GAGTICCCCT TAITIGAAAAT GGAATGATTG AGCGGATGAT TGAGAAGCTG TTTCCGTGCG TGATCCTCAC CCCCCTCGAC TGCTTCTGGG AGGGAGCCAA CTCAAGGGGA ATAACTITITA CCITACTAAC ICGCCTACTA ACTCITCGAC AAAGGCACGC ACTAGGAGTG GGGGGAGCTG ACGAAGACCC ICCCTCGGIT 201

TGAGGTTCCC CCGAGGCGGA TGGACGGCGA GGGTTACACC GA®TGCTCGA CTCACCCCCG ACGGTACCGA AGAGGGTGTT TAAGTACGTG ACCGTCCTCC 301 ACTCCAAGGG GGCTCCGCCT ACCTGCCGCT CCCAATGTGG CTCACGAGCT GAGTGGGGGC TGCCATGGCT TCTCCCACAA ATTCATGCAC

401 AATTIGCTIGCT GGGAGGCATG GCCAGAGAGC CCCAAGGAGA GCTGCTGAGG GCAGAGGCCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCCC GCCAGCTGTA TTAACGACGA, CCCTCCGTAC, CGGTCTTGG, GGGTTCCTCT, CGACGACTCC, CGTCTCCGGG, ACGTCTCGTG, GAAGAACGAC, TACTCAGGGG, CGGTCGACAT

501 CGAGCATTIC CGGGGTGACT ATCAGACACA TGACATTGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGGCGCTT TGTGCAGGTC GCTCGTAAAG GCCCCACTGA TAGTCTGTGT ACTGTAACCG ACCTCACTCC TCGTCCGGTC GTGTCACGAT GTTCGGACCG TCGCCGCGAA ACACGTCCAG

601 GGTAIGGACA AGGACAGGGG GGIGCCCIGA GGCCAIICCC ICCICCIGCC CCCICCIAIC CACCCIGIII CICCAGCIGG CCCAGGAGGC CCIGCCIGAG CCATACCTGT TCCTGTCCCC CCACGGGACT CCGGTAAGGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTCGACC GGGTCCTCCG GGACGGACTC

TTGCGAAGGG TCGTCTAGGT ACGSAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACGC AAGAGACTTC AGTCACGACG GGCACACCAC CCTCCGATAG 701 AACGCTICCC AGCAGAICCA IGCCTICTCC ICCACCACCC IGGAIGACAI CCIGCAIGCG ITCICIGAAG ICAGIGCIGC CCGIGIGGIG GGAGGCTAIC

801 IGCICAIGGI GGGICTIGCA CCIGGCACCI IGCCCCCACC CCACCICCAA CCAGIGCCCA CCCIGGGGAG CCCCIGAGAC IGCCCTITICC CCCCACAGCI ACGAGTACCA CCCAGAACGT GGACCGTGGA ACGGGGGTGG GGTGGAGGTT GGTCACGGGT GGGACCCCTC GGGGACTCTG ACGGGAAAGG GGGGTGTCGA

### 23/27 1/23 e

ICGGATACGG ACACACTGGT ACGACGCCAC CCTGACGCGG GTCAGGGTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG CCACCGGAGT GGCCTATGCC TGTGTGACCA TGCTGCGGTG GGACTGCGCC CAGTCCCAGG GTTCCGTGGG CCTTGCCGGG GTACTGCTGG TGGCCCTGGC GGTGGCCTCA 901

CAGGACTGCA GGGCAGACTC AGTGCCAGTC ACCAGGCTTC CCGGAACCCG AGACACGGGA CGAGCCGTAG TGGAAGTTAC GACGGTGATG GGTCCATGCG GTCCTGACGT CCCGTCTGAG TCACGGTCAG TGGTCCGAAG GOCCTTGGGC TCTGTGCCCT GCTCGGCATC ACCTTCAATG CTGCCACTAC CCAGGTACGC 1001

CATGCCTTCA IGCCCAGGAG TCGACGGGCG AGGAGACGGG GAGGICCACG ACGGGAAGAA CTGAGACCCT TAGCCGCACC TACTGCATAA GGACGACCGC ACGGGTCCTC AGCTGCCCGC TCCTCTGCCC CTCCAGGTGC TGCCCTTCTT GACTCTGGGA ATCGGCGTGG ATGACGTATT CCTGCTGGCG 1101

GGTTCAAGTG GTCTCCGAGA CGGACCGTGG GGAGAGGTCC ACCCCGGAAC AGGGGGTCCC GAGTAGACTC CGTCGAGTCG AATGACCAAT TCTCGGAGAA CCAAGTTCAC CUTUTUCAGG TGGGGCUTTG TCCCCCAGGG CTCATCTGAG GCAGCTCAGC TTACTGGTTA AGAGCCTCTT CAGAGGCTCT GCCTGGCACC 1201

GCTAATGAAC CTCGGTGCCT CTTGTCCCCA TGTGTAAACA GGGGAAATAA TAGTGCTGTG TCCTAAGGGT TATTGTTTGG ATCAGTGAAG TGGAACCCGA CGATTACTTG GAGCCACGGA GAACAGGGGT ACACATTTGT CCCCTTTATT ATCACGACAC AGGATTCCCA ATAACAAACC TAGTCACTTC ACCTTGGGCT 1301

TAACTCAAGT TGAATGCTTA GAACAGCCCA TCATACGTAC ATGGTACCCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCCAAGTT ATTGAGTICA ACTIACGAAT CTTGTCGGGT AGTATGCATG TACCATGGGT TATTTACGAT CGGTGACACA ATACTGACGG GGTGGAGACG TGGGGTTCAA 1401

GGACTCGGAG GGGAAGTGAG GTGAAACTGT GCCGGGGAGG GACACTGGA CTCCCGTCCA GGGGTGAGAC AGGACCGTCC TCGCGTACCC GCTCACAGAC COUTICACTO CACTITIGACA CGGCCCCTCC CITGIGACCI GAGGGCAGGI CCCCACTOTG ICCIGGCAGG AGCGCAIGGG CGAGIGICIG CCTGAGCCTC 1501

GCCTTCTCCC GTCGCGTGCC CGTGGTCACA ACÀTGAGTGT AGGTAGTTGT TGTACCGGCG GAAGGAGTAC CGACGGGAGC AAGGGTAGGG ACGCGACGCT CGGAAGAGGG CAGCGCACGG GCACCAGTGT TGTACTCACA TCCATCAACA ACATGGCCGC CTTCCTCATG GCTGCCCTCG TTCCCATCCC TGCGCTGCGA 1601

ATGTCGGACC TGGATGCCGC CGCGGTGACG GTCGCGGAAC TACACGAGAC GACGAAGAGG TCCATGACGG ACGCGGGGTC GGGGAAGGAG GGCACTGGGT CCGTGACCCA ACCTACGGCG GCGCCACTGC CAGCGCCTTG ATGTGCTCTG CTGCTTCTCC AGGTACTGCC TGCGCCCCAG CCCCTTCCTC TACAGCCTGG 1701

TECECTEACE AGEATITEAA GGEACAGACE TGICAICEAE IETETACEIE ITECAGIECE IGCICIGEIE AGGIGAIIEA GAIECIGEEC GCGGTCGGAC AGGGGAGTGG TCGTAAAGTT CGCCAGCCTG 1801

AGTACCAGTG GGCATTGCCC ACCTCACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGGTCA GTACACCAGT CCCTGCCCTG TCATGGTCAC CCGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAAATGGG TGACACTTCG GTCGTCGGTC GGGACGGGAC GTCCTCGACC CAGGAGCTGG 1901

GETAGGACGG AGGGGTTCGG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAAGTCGGG ACCTCCCAGG TGTGCCCTGG AAGATCCGGT TTCTAGGCCA CCATCCTGCC TCCCCAAGCC CACCTGGTGC CCCCACCTTC TGACCCACTG GGCTCTGAGC TCTTCAGCCC TGGAGGGTCC ACACGGGACC 2001

# FIG. 10B

GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCTG CCCTGTGCGC GCTGGAATCT TGCCCATTTC GCCCGCTATC AGTTTGCCCC GTTGCTGCTC SCTECTECTE TETTECETET TECGTEGGAE GITEAGGGAE GGGAEAEGGG CGAEETTAGA AEGGGIAAAG EGGGEGATAG TEAAAEGGGG CAAEGAEGAG

GCCCTGACGG GETTCCGGTA GCACGACCAC GAGAAGCCAC GAGAAGACCC GGACTCGGAĠ ATGCCTCGGT GGAACCACGT TCTGCCGGAC CGGGACTGCC CCAAGGCCAT CGTGCTGGTG CTCTTTGGTG CTCTTCTGGG CCTGAGGCTC TACGGAGCCA CCTTGGTGCA AGACGGCCTG GTCAGTGTAC 2201 CAGTCACATG

ATGTEGTECC TCGGGGCACC AAGGAGCATG CCTTCCTGAG CGCCCAGCTC AGGTACTTCT CCCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA TACACCACGG AGCCCCGTGG TTCCTCGTAC GGAAGGACTC GCGGGTCGAG TCCATGAAGA GGGACATGCT CCACCGGGAC CACTGGGTCC CACCGAAACT 2301

GATGCGGGTG AGGETTGCGC GGGAGAACT AGACGTGGTC GCGAAGTCAA GGGAGTTCCG CCACGACGGG GGTGGCCGGT GGGTCCGTGG GGCGTGGACC TOCCAAGGGG COCTOTITGA ICIGCACCAG CGCIICAGII COCTOAAGGC GGIGCIGCCG CCACCGGCCA CCCAGGCACC CTACGCCCAC 2401

GACCTGATAA TGGCGTTGAC CGATGTCCCT TAGGTCCGAC GGAAACTGGT CCTGACCCGGA AGACCCGCGT AGTGGGCGGT GAGCATGGCG TTACCGAGAC GGACTGGGCT TCTGGGCGCA TCACCCGCCA CTCGTACCGC AATGGCTCTG CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA 2501

GGTCCACTAG TCCTACCCCG GGACCGGATG TTCGACGAGT AGGTCTGACC TCTGCGGGTC CTCGGAGACC TAAAGTCGGT CCAACCCTCT CCGACCTCC CCAGGTGATC AGGATGGGGC CCTGGCCTAC AAGCTGCTCA TCCAGACTGG AGACGCCCAG GAGCCTCTGG ATTTCAGCCA GGTTGGGAGA GGGCTGGAGG 2601

ATGTCCCCGA CGTCCGGAGG ACCCGGGTCC GGAAGTCGGG AGAGACGGAG ACGTCGACTG GTGTTCCTTC GACCACCTGT CTCTCCCTGA CTAAGGTGGG 2701 TACAGGGCT GCAGGCCTCC TGGGCCCCAGG CCTTCAGCCC TCTCTGCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGGACT GATTCCACCC

GACCGTGTGG GTGAGCAGTG ACCCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCCT GAATGGCTGC CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGGACCC AGACCGTCGG AGTGTCCGGT TGAAGATGGG GGGTGGAGGA CTTACCGACG ACATGGGGCT 2801 GAGCTCTTCT

AGCCTGAGGC TGCTGTTTAT GCTGTGGTGC CCCCTCTTGG AAGCGTCACT CAGAACCCCC CTCGAGCGGA TCTCGGAGTC GGAGCGGGTG TGTTCGGGAC TCGGACTCG 2901 ACGACAAATA CGACÁCCACG GGGGAGAACC TTCGCAGTGA GTCTTGGGGG GAGCTCGGCA AGAGCCTCAG CCTCGCCCAC ACAAGCCCTG

CICACCECCC TGICCCTICIC CCICITICIC CITCCCCICC CCICCACAGI CCCGCCAGCI CAGCCCTIGG AGITIGCCCA GGACGGGTGA GACGGGGCAC GAGTGGCGGG ACAGGGAGAG GGAGAAGAGG GAAGGGGAGG GGAGGTGTCA GGGCGGTCGA GTCGGGAACC TCAAACGGGT 3001 CCTGCCCACT CTGCCCCGTG

FIG. 10C

CAAGGGGAAG GACGACGCAC CGGAGGTCTT CTGACGTCTG AAACACCTCC GGTAGCTCCC CCGGGCCCGT CGTACGCGTC TCCGGCCGGT CCGACCCCAC GGCTGGGGTG CTGCTGCGTG GCCTCCAGAA GACTGCAGAC TTTGTGGAGG CCATCGAGGG GGCCCGGGCA GCATGCGCAG AGGCCGGCCA GTTCCCCTTC 3101

GTGTGCACTT GTGCGGATGG GGTCGCCGAG GGGGAAGGAG AAGACCCTTG TCATAGACCC GGACGCCGCG ACGAAGGACG ACGGGCAGAC GTAGGACGAC CACACGTGAA cerecesese recrucerse rescentra careers AGTATCTGGG CACGCCTACC CCAGCGGCTC CCCCTTCCTC TTCTGGGAAC 3201

TCTCGTCTG TSCTCTGCTG CTCCTCAACC CCTGGACGGC TGGCCTCATA GTGAGTGCTT GCAGGAGTGG GGACAGAGAC ACCCCACCCT TCCCTGCCCA AGGAGCAGAC ACGAGACGAC GAGGAGTTGG GGACCTGCCG ACCGGAGTAT CACTCACGAA CGTCCTCACC CCTGTCTCTG TGGGGTGGGA AGGGACGGGT 3301

CCTCGGGAGA CACTCGGGAC AGAGGGAGTC CACGACCAGG ACCGCTACTA CTGTCACCTT GAGAAACCAT AGTACCCAAA GECTGTEATE CETECTGEEA GGAGECETET GIGAGECETG TETECETEAG GIGETGGIEC IGGEGAIGAT GACAGIGGAA CICTIIGGIA ICAIGGGITI CGGACAGTAG GGAGGACGGT 3401

GAGCACGGGC GGACCCGTAG TTCGACTCAC GGTAGGGGCA CCACTAGGAA CACCGGAGAC ATCCGTAACC GCAACTCAAG TGTCAGGTGC ACCGAGACCA CTCGTGCCCG CCATCCCCGT GGTGATCCTT GTGGCCTCTG TAGGCATTGG CGTTGAGTTC ACAGTCCACG TGGCTCTGGT AAGCTGAGTG CCTGGGCATC 3501

CTGGGTGGAC TGGGGCCCCT CCCTGGTTAG TCGACTAAGT CATAAGTTGT GTATAACAAG TTCGGGGATG ATACACGATC CATGATAAAT TCTTAAACCC GACCCACCTG ACCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTTC AAGCCCCTAC TATGTGCTAG GTACTATTTA AGAATTTGGG 3601

GIGGIGECTO ATTOCTGTAA TOCCAGOACT TIGGGAGGCO GAGGOGGTG GATCACOTGA GGTOGGGAGT TOGAAACCAG COTGGCCAAC ATGGTGAAAC CACCACCGAG TAAGGACATT AGGGTCGTGA AACCCTCCGG CTCCGCCCAC CTAGTGGACT CCAGCCCTCA AGCTTTGGTC GGACCGGTTG TACCACTTTG 3701

TGAACCTGGG GGACAGAAAT GATTITIATG TITITIAATC GGTCCGCACC ACCGTGTACG GTCATCAGGG TCGATGAAAC CTCCGACTCC GTCTTAACGA ACTTGGACCC CTAAAAATAC AAAAAATTAG CCAGGCGTGG TGGCACATGC CAGTAGTCCC AGCTACTTTG GAGGCTGAGG CAGAATTGCT CCTGTCTTA 3801

AAGGGCGGCC AGGCGAAGGT TGCAGTGAGC TGAGATCGTG CCATTGCACT CCAGCCTGGG CAACAAGAGT GCAACTCTCC GTCTCAAAAA AAAAAAAAA ICCECTICCA ACGICACTOG ACTOTAGGAG GGIAACGIGA GGICGGACCO GIIGITICICA CGIIGAGAGG CAGAGIIIII IIIIIIIII 3901

4001 GCGA

4

LUGU

FIG. 10D

1 TICCGGCATG ACTCGATCGC CGCCCTCAG AGAGCTGCCC CCGAGTTACA CACCCCCAGC TCGAACCGCA GCACCCCAGA TCCTAGCTGG GAGCCTGAAG AAGGCCGTAC TGAGCTAGCG GCGGGGAGTC TCTCGACGGG GGCTCAATGT GTGGGGGTCG AGCTTGGCGT CGTGGGGTCT AGGATCGACC

CGAGGTGAGA CCGAAGCACG AATGAAGGTC CCGGACGAGA AGAGAGACCC TACGCCCTÀG GTCTCTGTAA CACCGTTTCA CGAGAAAGAC CCTGACAACC GGACTGTTGG GCTCTTTCTG GETECACTET GGETTEGTGE TIACTICEAG GGEETGETET TETETEGGG AIGCGGGAIC CAGAGACAIT GIGGCAAAGI 101

GGACCGTAAT CCAGAGGCGT ACCGGTAATA ACTCTGTTTG AACCTTGTCG AGACCCATCT TCACCCGTCG GCCCACTCGG TCCTCGACGT 201 CCTTTGGGGC CCTGGCATTA GGTCTCCGCA TGGCCATTAT TGAGACAAAC TTGGAACAGC TCTGGGTAGA AGTGGGCAGC CGGGTGAGCC AGGAGCTGCA GGAAACCCCG THACACCAAG GAGAAGCTGG GGGAGGAGGC TGCATACACC TCTCAGATGC TGATACAGAC CGCACGCCAG GAGGGAGAGA ACATCCTCAC ACCCGAAGCA AATGIGGITC CICTTCGACC CCCTCCTCCG ACGIAIGIGG AGAGICIACG ACTAIGICIG GCGIGCGGIC CICCCICICI IGIAGGAGIG IGGGCTTCGI 301

CITGGCCTCC ACCTCCAGGC AGCCCTCACT GCCAGIAAAG ICCAAGIATC ACTCIAIGGG AAGICCTGGG AITTGAACAA AAICTGCIAC AAGICAGGAG GAACCGGAGG TGGAGGTCCG TCGGGAGTGA CGGTCATTTC AGGTTCATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG TTCAGTCCTC 401

TICCCCTIAT TGAAAATGGA ATGATTGAGT GGATGATTGA GAAGCTGTTT CCGTGCGTGA TCCTCACCCC CCTGGACTGC TTCTGGGAGG GAGCCAAACT AAGGGAATA ACTITIACCI TACIAACICA CCIACIAACI CIICGACAAA GGCACGCACI AGGAGIGGGG GGAGCIGACG AAGACCCICC CICGGIIIIGA 501

SGTTCCCCCG AGGCGGATGG ACGGGCCGGC GGGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGGAGGGAA CCAAGGGGG TCCGCCTACC TGCCCGGCCG CCCGGATATC CAGTGGACCA ACCTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCTT 601

GAGGECTTCE GGGAGCTGCT AGACAAGGCA CAGGTGGGCC AGGCCTACGT GGGCGGCCC TGTCTGCACC CTGATGACCT CCACTGCCCA CCTAGTGCCC CTCCCGAAGG CCCTCGACGA TCTGTTCCGT GTCCACCCGG TCCGGATGCA CCCGGCGGG ACAGACGTGG GACTACTGGA GGTGACGGGT GGATCACGGG 701

CCAACGATCA CAGCAGGCAG GCTCCCAATG TGGCTCACGA GCTGAGTGGG GGCTGCCATG GCTTCTCCCA CAAATTCATG CACTGGCAGG AGGAATTGCT SOTTGGTAGT GICGICCGIC CGAGGGTTAC ACCGAGTGCI CGACICACCC CCGACGGIAC CGAAGAGGGI GITIAAGIAC GIGACCGICC ICCTIAACGA 801

CGACCCTCCG TACCGGTCTC TGGGGGTTCC TCTCGACGAC TCCCGTCTCC GGGACGTCTC GTGGAAGAAC GACTACTCAG GGGCGGTCGA CATGCTCGTA 901 GCTGGGAGGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGGCAGAGG CCCTGCAGAG CACCTTCTTG CTGATGAGTC CCCGCCAGCT GTACGAGCAT

TICCGGGGIG ACTAICAGAC ACAIGACAII GGCIGGAGIG AGGAGCAGGC CAGCACAGIG CIACAAGCCI GGCAGCGGCG CIIIGIGCAG CIGGCCCAGĞ AAGGCCCCAC TGATAGTCTG TGTACTGTAA CCGACCTCAC TCCTCGTCCG GTCGTGTAC GATGTTCGGA CCGTCGCCGC GAAACACGTC GACCGGGTCC 1001

recenter saagreagie creceerer TECGGGACGG ACTETTGEGA AGGGTEGTET AGGTACGGAA GAGGAGGTGG TGGGAECTAT TGTAGGACGT ACGCAAGAGA ETTEAGTEAE GACGGGCACÁ ACATCCTGCA ACCCTGGATA CTCCTCCACC AGGCCCTGCC TGAGAACGCT TCCCAGCAGA TCCATGCCTT 1101

1201 GGTGGGAGGC TATCTGGTCA TGCTGGCCTA TGCCTGTGTG ACCATGCTGC GGTGGGACTG CGCCCAGTCÇ CAGGGTTCCG TGGGCCTTGC CGGGGTACTG CCACCTCCG ATAGACGAGT ACGACCGGAT ACGGACACAC TGGTACGACG CCACCCTGAC GCGGGTCAGG GTCCCAAGGC ACCCGGAACG GCCCCATGAC

TTACGACGGT GATGGGTCCA CGACGGGAAG AACCGAGACC CTGGTGGCCC TGGCGGTGGC CTCAGGCCTT GGGCTCTGTG CCCTGCTCGG CATCACCTTC AATGCTGCCA CTACCAGGT GCTGCCCTTC GACCACCGGG ACCGCCACCG GAGTCCGGAA CCCGAGACAC GGGACGAGCC GTAGTGGAAG 1301

TGCAGCGCAC CTTAGCCGCA CCTACTGCAT AAGGACGACC GCGTACGGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGCGTAC CCGCTCACAG ACGTCGCGTG CACAGAGGCT CTGCCTGGCA CCCCTCTCCA GGAGCGCATG GGCGAGTGTC CGCATGCCTT GAATCGGCGT GGATGACGTA TTCCTGCTGG 1401

CTTACAGCCA CCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCGG CGGAAGGAGT ACCGACGGGA GCAAGGGTAG GGACGCGACG CTCGGAAGAG GAATGTCGGT GGGCACCAGT GTCGTACTCA CATCCATCAA CAACATGGCC GCCTTCCTCA TGGCTGCCCT CGTTCCCATC CCTGCGCTGC GAGCCTTCTC 1501

TOCTCAGECT GGACCTACGG CGGCGCCACT GCCAGCGCCT TGATGTGCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCA AGGAGTOGGA CCTGGATGCC GCCGGGGGGA CGGTCGCGGA ACTACACGAG ACGACGAAGA GGTCAGGGAC GAGACGAGTC CACTAAGTCT AGGACGGGGT 1601

GGAGCTGGGG GACGGGACAG TACCAGTGGG CATTGCCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGGTCACC ACACCAGTGG GIAACGGGIG GAGIGACGGI GICAAGIICG GAAAIGGGIG ACACIICGGI CGICGGICGI CCTCGACCCC CTGCCCTGTC ATGGTCACCC 1701

CCACCTICIG ACCCACTGGG CTCTGAGCTC ITCAGCCCTG GAGGGTCCAC ACGGGACCTT CTAGGCCAGG TAGGACGÓAG GOGTTCGGGT GGACCACGGG GGTGGAAGAC TGGGTGÁCCC GAGACTCGAG AAGTCGGGAC CTCCCAGGTG TGCCCTGGAA GATCCGGTCC CCTGGTGCCC ATCCTGCCTC CCCAAGCCCA 1801

AAGGCAGAAG GCAGCCTGCA AGTCCCTGCC CTGTGCCCGC TGGAATCTTG CCCATTTCGC CCCGGAATTC CTGCAGCCCG GGGATCCAC TICCGICTIC CGICGGACGI ICAGGGACGG GACACGGGCG ACCTIAGAAC GGGIAAAGCG GGGCCTIAAG GACGICGGGC, CCCCTAGGIG AGGAGGAGAC TCCTCCTCTG 1901

E A TAGTICTAGA GCGGCCGCCA CCGCGGTGGA GCTCCAGCTT TTGTTCCCTT TAGTGAGGGT TAATTGCGCG CTTGGGTATC ATCAAGATCT CGCCGGCGGT GGCGCCACCT CGAGGTCGAA AACAAGGGAA ATCACTCCCA ATTAACGCGC GAACCCATAG 2001

# FIG. 11B

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